(FILE 'HCAPLUS' ENTERED AT 11:33:30 ON 28 APR 2004)
L1 1856 SEA FILE=HCAPLUS ABB=ON PLU=ON HUMAN?(S)(CHROMOSOME(1W) 13)
L6 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND SECRET?
L7 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND (PROTEIN OR POLYPROTEIN OR PEPTIDE OR POLYPEPTIDE)

-Key terms

L7 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 24 Apr 2003
ACCESSION NUMBER: 2003:314665 HCAPLUS
DOCUMENT NUMBER: 139:34261
TITLE: Genome-wide copy number imbalances identified in familial and sporadic medullary thyroid carcinoma
AUTHOR(S): Marsh, Deborah J.; Theodosopoulos, George; Martin-Schulte, Klaus; Richardson, Anne-Louise; Philips, Jeanette; Roher, Hans-Dietrich; Delbridge, Leigh; Robinson, Bruce G.
CORPORATE SOURCE: Cancer Genetics, Kolling Institute of Medical Research, Royal North Shore Hospital, St. Leonards, 2065, Australia
SOURCE: Journal of Clinical Endocrinology and Metabolism (2003), 88(4), 1866-1872
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Medullary thyroid carcinoma (MTC) is a malignant tumor of the calcitonin-**secreting** parafollicular C cells of the thyroid occurring sporadically and as a component of the multiple endocrine neoplasia type 2/familial medullary thyroid carcinoma syndrome. The primary genetic cause of multiple endocrine neoplasia type 2 is germline mutation of the RET protooncogene. Somatic point mutations in RET also occur in sporadic MTC. Although RET mutation is likely sufficient to cause C-cell hyperplasia, the precursor lesion to MTC, tumor progression is thought to be due to clonal expansion caused by the accumulation of somatic events. Using the genome-scanning technique comparative genomic hybridization, we identified chromosomal imbalances that occur in MTC including deletions of chromosomes 1p, 3q26.3-q27, 4, 9q13-q22, 13q, and 22q and amplifications of chromosome 19. These regions house known tumor suppressor genes as well as genes encoding subunits of the multicomponent complex of glycosylphosphatidylinositol-linked **proteins** (glial cell line-derived neurotrophic factor family receptors α-2-4) and their ligands glial cell line-derived neurotrophic factor, neurturin, persephin, and artemin that facilitate RET dimerization and down-stream signaling. Chromosomal imbalances in the MTC cell line TT were largely identical to those identified in primary MTC tumors, consolidating its use as a model for studying MTC.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 23 Feb 2003

ACCESSION NUMBER: 2003:134659 HCAPLUS
DOCUMENT NUMBER: 138:380082
TITLE: Genomic scan of glucose and insulin metabolism phenotypes: The HERITAGE Family Study
AUTHOR(S): An, Ping; Hong, Yuling; Weisnagel, S. John; Rice, Treva; Rankinen, Tuomo; Leon, Arthur S.; Skinner, James S.; Wilmore, Jack H.; Chagnon, Yvon C.; Bergman, Richard N.; Bouchard, Claude; Rao, D. C.
CORPORATE SOURCE: Division of Biostatistics, and the Departments of Genetics and Psychiatry, Washington University School of Medicine, St Louis, MO, 63110-1093, USA
SOURCE: Metabolism, Clinical and Experimental (2003), 52(2), 246-253
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Genetic factors play a role in the regulation of glucose metabolism-related traits such as insulin sensitivity (SI), insulin **secretion**, and glucose effectiveness (SG). Several genomic scans have been performed to localize genes involved in glucose metabolism-related traits. However, few of these studies have been performed with phenotypes derived from the frequently sampled i.v. glucose tolerance test (IVGTT) using the minimal modeling (MINMOD) approach. Here, we report on such a scan for glucose metabolism-related traits derived from MINMOD anal. of IVGTT data in 322 sibling pairs from 95 sedentary white families and 75 sibling pairs from 49 sedentary black families from the HERITAGE Family Study. In addition to SI and SG, we also considered acute insulin response to a glucose challenge (AIRGlucose), which is an index for insulin **secretion**, and disposition index (DI, product of SI and AIRGlucose), which is a measure of the activity of pancreatic β cells corrected for insulin resistance. These traits were adjusted for age, sex, and body mass index (BMI) in each of 8 sex-by-generation-by-race groups, and then standardized residuals were used as the phenotypes in the linkage analyses. Analyses were with the multipoint variance components linkage method, as implemented in the computer program SEGPATH, using 509 markers. Several regions with promising linkages (LOD score ≥ 1.75, P ≤ .0023) were detected. They include five regions (1q41 and 8p23.2 for SI, 4q32.1 and 10p15.3 for AIRGlucose, and 13q32.1 for DI) in whites and 2 regions (9p11.2 for SG and 10q26.11 for SI) in blacks. Three of these regions (4q32.1, 9p11.2, 10p15.3) are likely to harbor genes that influence interindividual variation in glucose metabolism-related traits as they replicate findings from other studies. Fine mapping and association studies of candidate genes within these genomic regions are warranted.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 20 Nov 2002
ACCESSION NUMBER: 2002:879021 HCAPLUS

DOCUMENT NUMBER: 138:23592
TITLE: Dendritic cell-associated lectin-1: a novel dendritic cell-associated, C-type lectin-like molecule enhances T cell **secretion** of IL-4
AUTHOR(S): Ryan, Elizabeth J.; Marshall, Aaron J.; Magaletti, Dario; Floyd, Helen; Draves, Kevin E.; Olson, N. Eric; Clark, Edward A.
CORPORATE SOURCE: Departments of Microbiology, and Regional Primate Research Center, University of Washington, Seattle, WA, 98195, USA
SOURCE: Journal of Immunology (2002), 169(10), 5638-5648
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have characterized dendritic cell (DC)-associated lectin-1 (DCAL-1), a novel, type II, transmembrane, C-type lectin-like **protein**. DCAL-1 has restricted expression in hemopoietic cells, in particular, DCs and B cells, but T cells and monocytes do not express it. The DCAL-1 locus is within a cluster of C-type lectin-like loci on **human chromosome** 12p12-**13** just 3' to the CD69 locus. The consensus sequence of the DCAL-1 gene was confirmed by RACE-PCR; however, based on sequence alignment with genomic DNA and with various human expressed sequence tags, the authors predict that DCAL-1 has two splice variants. C-type lectins share a common sequence motif of 14 invariable and 18 highly conserved aa residues known as the carbohydrate recognition domain. DCAL-1, however, is missing three of the cysteine residues required to form the standard carbohydrate recognition domain. DCAL-1 mRNA and **protein** expression are increased upon the differentiation of monocytes to CD1a+ DCs. B cells also express high levels of DCAL-1 on their cell surface. Using a DCAL-1 fusion **protein** the authors identified a population of CD4+ CD45RA+ T cells that express DCAL-1 ligand. Coincubation with soluble DCAL-1 enhanced the proliferation of CD4+ T cells in response to CD3 ligation and significantly increased IL-4 **secretion**. In contrast, coincubation with soluble DC-specific ICAM-3-grabbing nonintegrin (CD209) fusion **protein** as a control had no effect on CD4+ T cell proliferation or IL-4 and IFN-γ **secretion**. Therefore, the function of DCAL-1 on DCs and B cells may act as a T cell costimulatory mol., which skews CD4+ T cells toward a Th2 response by enhancing their **secretion** of IL-4.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Nov 2002
ACCESSION NUMBER: 2002:847394 HCAPLUS
DOCUMENT NUMBER: 138:216106
TITLE: A locus on human chromosome 20 contains several genes expressing protease inhibitor domains with homology to whey acidic **protein**
AUTHOR(S): Clauss, Adam; Lilja, Hans; Lundwall, Ake

CORPORATE SOURCE: University Hospital MAS, Department of Laboratory Medicine, Wallenberg Laboratory, Lund University, Malmoe, S-205 02, Swed.
SOURCE: Biochemical Journal (2002), 368(1), 233-242
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A locus containing 14 genes, encoding **protein** domains that have homol. with whey acidic **protein** (WAP), has been identified in a region of 678 kb on **human** **chromosome** 20q12-**13**.1. Among them are genes of the known or postulated protease inhibitors elafin, **secretory** leukocyte protease inhibitor, human epididymis gene product 4, eppin, and huWAP2. Nucleotide sequences of full-length transcripts were obtained from cDNA fragments generated by rapid amplification of cDNA ends. Characteristic features of the genes are that the upstream promoter regions are devoid of TATA-boxes and that the coding nucleotides are divided into distinct exons for the signal **peptide** and for each WAP domain. In most cases, there is also a sep. exon encompassing a few terminal codons and the 3' untranslated nucleotides. There are also examples of mixed type inhibitors, that encode inhibitor domains of both WAP and Kunitz types. Several of the genes appear to be expressed ubiquitously, but, in most cases, the highest transcript levels are found in epididymis followed by testis and trachea. Some of the genes also display high transcript levels in neural tissues. Potential biol. roles of **protein** products could be in host defense against invading micro-organisms or in the regulation of endogenous proteolytic enzymes, of which those originating from the kallikrein gene locus on chromosome 19 are of particular interest.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 02 Sep 2002
ACCESSION NUMBER: 2002:660099 HCAPLUS
DOCUMENT NUMBER: 137:368054
TITLE: Chediak-Higashi syndrome: a rare disorder of lysosomes and lysosome related organelles
AUTHOR(S): Shiflett, Shelly L.; Kaplan, Jerry; McVey Ward, Diane
CORPORATE SOURCE: Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT, USA
SOURCE: Pigment Cell Research (2002), 15(4), 251-257
CODEN: PCREEA; ISSN: 0893-5785
PUBLISHER: Blackwell Munksgaard
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Chediak-Higashi Syndrome (CHS) is a rare autosomal recessive disorder characterized by severe immunol. defects including recurrent bacterial infections, impaired chemotaxis and abnormal natural killer (NK) cell function. Patients with this syndrome exhibit other symptoms such as an associated lymphoproliferative syndrome, bleeding tendencies, partial albinism

and peripheral neuropathies. The classic diagnostic feature of CHS is the presence of huge lysosomes and cytoplasmic granules within cells. Similar defects are found in other mammals, the most well studied being the beige mouse and Aleutian mink. A positional cloning approach resulted in the identification of the Beige gene on **chromosome 13** in mice and the CHS1/LYST gene on chromosome 1 in **humans**. The **protein** encoded by this gene is 3801 amino acids and is highly conserved throughout evolution. The identification of CHS1/Beige has defined a family of genes containing a common BEACH motif. The function of these **proteins** in vesicular trafficking remains unknown.

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 21 Jul 2002
ACCESSION NUMBER: 2002:540978 HCAPLUS
DOCUMENT NUMBER: 137:123913
TITLE: Cutting edge: IL-17D, a novel member of the IL-17 family, stimulates cytokine production and inhibits hemopoiesis
AUTHOR(S): Starnes, Trevor; Broxmeyer, Hal E.; Robertson, Michael J.; Hromas, Robert
CORPORATE SOURCE: Departments of Medicine and Biochemistry, Walther Oncology Center, Indiana University Medical Center, Indianapolis, IN, 46202, USA
SOURCE: Journal of Immunology (2002), 169(2), 642-646
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel cytokine termed IL-17D was cloned using nested RACE PCR. It is a **secreted** cytokine with homol. to the IL-17 family of **proteins**. IL-17D is preferentially expressed in skeletal muscle, brain, adipose tissue, heart, lung, and pancreas. Treatment of endothelial cells with purified rIL-17D **protein** stimulated the production of IL-6, IL-8, and GM-CSF. The increased expression of IL-8 was NF-κB-dependent. RIL-17D also demonstrated an inhibitory effect on hemopoiesis of myeloid progenitor cells in colony formation assays.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 Dec 2001
ACCESSION NUMBER: 2001:897056 HCAPLUS
DOCUMENT NUMBER: 136:380968
TITLE: Identification and characterization of a novel family of mammalian ependymin-related **proteins** (MERPs) in hematopoietic, nonhematopoietic, and malignant tissues
AUTHOR(S): Apostolopoulos, Jim; Sparrow, Rosemary L.; McLeod, Janet L.; Collier, Fiona M.; Darcy, Phil K.; Slater, Howard R.; Ngu, Con; Gregorio-King,

Claudia C.; Kirkland, Mark A.
CORPORATE SOURCE: Research Unit, Australian Red Cross Blood Service-Victoria, Victoria, Australia
SOURCE: DNA and Cell Biology (2001), 20(10), 625-635
CODEN: DCEBE8; ISSN: 1044-5498
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Evidence is presented for a family of mammalian homologs of ependymin, which we have termed the mammalian ependymin-related **proteins** (MERPs). Ependymins are **secreted** glycoproteins that form the major component of the cerebrospinal fluid in many teleost fish. We have cloned the entire coding region of human MERP-1 and mapped the gene to chromosome 7p14.1 by fluorescence in situ hybridization. In addition, three human MERP pseudogenes were identified on chromosomes 8, 16, and X. We have also cloned the mouse MERP-1 homolog and an addnl. family member, mouse MERP-2. Then, using bioinformatics, the mouse MERP-2 gene was localized to chromosome 13, and we identified the monkey MERP-1 homolog and frog ependymin-related **protein** (ERP). Despite relatively low amino acid sequence conservation between piscine ependymins, toad ERP, and MERPs, several amino acids (including four key cysteine residues) are strictly conserved, and the hydropathy profiles are remarkably alike, suggesting the possibilities of similar **protein** conformation and function. As with fish ependymins, frog ERP and MERPs contain a signal **peptide** typical of **secreted proteins**. The MERPs were found to be expressed at high levels in several hematopoietic cell lines and in nonhematopoietic tissues such as brain, heart, and skeletal muscle, as well as several malignant tissues and malignant cell lines. These findings suggest that MERPs have several potential roles in a range of cells and tissues.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 May 2000
ACCESSION NUMBER: 2000:314725 HCAPLUS
DOCUMENT NUMBER: 132:330629
TITLE: Cloning and cDNA sequences of novel TNF family members, DRL, and uses for modulating apoptosis or immune response
INVENTOR(S): Lenardo, Michael J.; Wang, Jin; Jiang, Di
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000026244 | A2 | 20000511 | WO 1999-US25954 | 19991104 |

WO 2000026244 A3 20001109
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-106976P P 19981104

AB The present invention provides an isolated nucleic acids encoding DRL (death receptor ligand) **proteins**, DRL-1 (or tumor necrosis factor (TNF)-like ligand) of human and mouse and DRL-2 of human. Unique fragments of DRLs, purified DRL **polypeptides**, and purified antibodies which bind to the DRL **protein** or fragments thereof are also provided. DRL-1 is a type 2 membrane **protein** having transmembrane and extracellular domains and predicted N-glycosylation site. The extracellular domain of DRL-1 has extensive homol. to other TNF family members. DRL-2 is another member of the TNF family, but the cDNA for DRL-2 does not encode an N-terminal hydrophobic stretch that would normally anchor a **protein** to the membrane. Thus, DRL-2 would be directly **secreted** into the extracellular medium. The DRL **polypeptides** can be used to stimulate an immune response or induce apoptosis. The DRL antibodies can be used to inhibit a T cell response, to inhibit apoptosis or to suppress an autoimmune response.

L7 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 27 Jan 2000
ACCESSION NUMBER: 2000:64913 HCAPLUS
DOCUMENT NUMBER: 132:320347
TITLE: Molecular abnormalities associated with **secretory** carcinomas of the breast
AUTHOR(S): Maitra, Anirban; Tavassoli, Fattaneh A.; Albores-Saavedra, Jorge; Behrens, Carmen; Wistuba, Ignacio I.; Bryant, David; Weinberg, Arthur G.; Rogers, Beverly B.; Saboorian, M. Hossein; Gazdar, Adi F.
CORPORATE SOURCE: Department of Pathology and Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical Center, Dallas, TX, 75235, USA
SOURCE: Human Pathology (1999), 30(12), 1435-1440
CODEN: HPCQA4; ISSN: 0046-8177
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Secretory** carcinomas (SCAs) represent a unique histol. variant of invasive breast carcinomas, occurring predominantly in patients younger than 30 yr of age. Data from limited series have shown SCAs to have a favorable prognosis in patients younger than 20 yr of age, whereas the clin. course tends to parallel the more common infiltrating ductal carcinomas (IDCs) in patients older than 20 yr. There are no reports on the mol. abnormalities associated with

this unusual tumor. Microdissected archival formalin-fixed tissue from 10 SCAs collected from 2 institutions were used to determine the frequencies of allelic loss at 13 chromosomal regions with 19 microsatellite markers, using multiplex polymerase chain reaction (PCR)-based techniques. The results of loss of heterozygosity (LOH) and microsatellite alterations (MAs) analyses were compared with 20 cases of IDCs. P53 gene mutation anal. was also performed on the 10 SCAs using single-strand conformation polymorphism (SSCP) anal., followed by sequencing of abnormal bands. LOH at multiple regions of chromosome 3p were the most common abnormality in both SCAs (55%) and IDCs (50%), followed by LOH at 17q21 (BRCA1 locus), 13q14 (retinoblastoma gene locus), and 8p21-23. No significant differences were seen in the frequencies of LOH at any chromosomal region except for 17p13 (p53 gene locus), where allelic losses were absent in SCAs, but evident in 46% of IDCs. The 2 histol. entities were similar in the fractional regional loss (FRL) index (0.26 v 0.24), fractional allelic loss (FAL) index (0.23 v 0.27), as well as in the frequency of MAs (0.015 v 0.005),. P53 gene missense mutation (G:C::A:T) was detected in 1 of 10 (10%) SCAs. Based on the considerable similarities in the mol. abnormalities associated with both tumors, the formation of secondary lumina in both the in situ and the invasive components, as well as suggestions from limited series that the clin. behavior in adult patients parallels that of IDCs, SCA most likely reflects a **secretory** variant of IDCs.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 21 Jun 1999
ACCESSION NUMBER: 1999:380488 HCAPLUS
DOCUMENT NUMBER: 131:169096
TITLE: BAFF, a novel ligand of the tumor necrosis factor family, stimulates B cell growth
AUTHOR(S): Schneider, Pascal; MacKay, Fabienne; Steiner, Veronique; Hofmann, Kay; Bodmer, Jean-Luc; Holler, Nils; Ambrose, Christine; Lawton, Pornsri; Bixler, Sarah; Acha-Orbea, Hans; Valmori, Danila; Romero, Pedro; Werner-Favre, Christiane; Zubler, Rudolph H.; Browning, Jeffrey L.; Tschopp, Jurg
CORPORATE SOURCE: Institute of Biochemistry, University of Lausanne, Epalinges, CH-1066, Switz.
SOURCE: Journal of Experimental Medicine (1999), 189(11), 1747-1756
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Members of the tumor necrosis factor (TNF) family induce pleiotropic biol. responses, including cell growth, differentiation, and even death. Here the authors describe a novel member of the TNF family, designated BAFF (for B cell activating factor belonging to the TNF family), which is expressed by T cells and dendritic cells. Human BAFF was mapped to chromosome 13q32-34. Membrane-bound BAFF was

processed and **secreted** through the action of a protease whose specificity matches that of the furin family of proprotein convertases. The expression of BAFF receptor appeared to be restricted to B cells. Both membrane-bound and soluble BAFF induced proliferation of anti-IgM-stimulated peripheral blood B lymphocytes. Moreover, increased amts. of Igs were found in supernatants of germinal center-like B cells costimulated with BAFF. These results suggest that BAFF plays an important role as costimulator of B cell proliferation and function.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 Feb 1999
ACCESSION NUMBER: 1999:96357 HCAPLUS
DOCUMENT NUMBER: 130:164008
TITLE: Cloning and cDNA sequence of **secreted protein** zsig46 encoded by **human chromosome 13**
INVENTOR(S): Sheppard, Paul O.; Gilbertson, Debra G.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9905275 | A1 | 19990204 | WO 1998-US15431 | 19980724 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9885898 | A1 | 19990216 | AU 1998-85898 | 19980724 |
| EP 1002077 | A1 | 20000524 | EP 1998-937110 | 19980724 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001511345 | T2 | 20010814 | JP 2000-504249 | 19980724 |
| US 2002042093 | A1 | 20020411 | US 1998-122383 | 19980724 |
| US 2002173624 | A1 | 20021121 | US 2001-10050 | 20011109 |

PRIORITY APPLN. INFO.:
US 1997-53613P P 19970724
US 1998-122383 A1 19980724
WO 1998-US15431 W 19980724

AB The present invention relates to polynucleotide and **polypeptide** mols. a for zsig46 **polypeptide**, a novel **secreted protein** located on **human chromosome 13**. The zsig46 **polypeptides** were initially identified by querying an EST database for

**secretory** signal sequences, characterized by an upstream methionine start site, a hydrophobic region of .apprx.13 amino acids and a cleavage site, in an effort to select for **secreted proteins**. Eight potential N-glycosylation sites and are located on zsig46, and potential post-translational processing sites are the dibasic sites at amino acids 38-39, 46-47, and 277-278. The mRNA corresponding to zsig46 is expressed predominantly in thyroid. The zsig46 **polypeptides**, and polynucleotides encoding them, are **secreted proteins** and may be used in the study of receptors for which a ligand has not yet been identified, of **secretory** pathways and the like. The present invention also includes antibodies to the zsig46 **polypeptides**.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 Jan 1999
ACCESSION NUMBER: 1999:52746 HCAPLUS
DOCUMENT NUMBER: 130:235634
TITLE: Netrin-1, Interaction with deleted in colorectal cancer (DCC) and alterations in brain tumors and neuroblastomas
AUTHOR(S): Meyerhardt, Jeffrey A.; Caca, Karel; Eckstrand, Bradley C.; Hu, Gang; Lengauer, Christoph; Banavali, Shripad; Look, A. Thomas; Fearon, Eric R.
CORPORATE SOURCE: Division of Molecular Medicine and Genetics and the Cancer Center, Departments of Internal Medicine, University of Michigan Medical Center, Ann Arbor, MI, 48109-0638, USA
SOURCE: Cell Growth & Differentiation (1999), 10(1), 35-42
CODEN: CGDIE7; ISSN: 1044-9523
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Netrins, a family of laminin-related **secreted proteins**, have critical roles in axon guidance and cell migration during development. The deleted in colorectal cancer (DCC) **protein** was implicated as a netrin-1 receptor component. The expression and function of netrins in adult tissues remain unknown, and direct interaction of netrin-1 with DCC was not demonstrated. The authors cloned the **human** netrin-1 (NTN1L) gene, mapped it to **chromosome** 17p12-**13**, and found that it encodes a 604 amino acid **protein** with 98% identity to mouse netrin-1 and 50% identity with the Caenorhabditis elegans UNC-6 **protein**. NTN1L transcripts were detected in essentially all normal adult tissues studied, and markedly reduced or absent NTN1L expression was seen in 50% of brain tumors and neuroblastomas. In 1 neuroblastoma, missense mutations at highly conserved NTN1L codons were found. Netrin-1 **protein** was cross-linked to DCC **protein** on the cell surface, but it did not immunoppt. with DCC in the absence of crosslinking and it failed to bind to a soluble fusion **protein**

containing the entire DCC extracellular domain. These findings demonstrating NTN1L loss of expression and mutations suggest that NTN1L alterations may contribute to the development of some cancers. The binding of netrin-1 to DCC appears to depend on the presence of a coreceptor or accessory **proteins**.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 06 Jan 1999
ACCESSION NUMBER: 1999:6317 HCAPLUS
DOCUMENT NUMBER: 130:163817
TITLE: Structure of the murine **secretory** leukoprotease inhibitor (Slpi) gene and chromosomal localization of the human and murine SLPI genes
AUTHOR(S): Kikuchi, Toshiaki; Abe, Tatsuya; Hoshi, Sachiko; Matsubara, Nobumichi; Tominaga, Yasuyuki; Satoh, Ken; Nukiwa, Toshihiro
CORPORATE SOURCE: Department of Respiratory Oncology and Molecular Medicine, Division of Cancer Control, Institute of Development, Aging and Cancer, Tohoku University, Sendai, 980-8575, Japan
SOURCE: American Journal of Respiratory Cell and Molecular Biology (1998), 19(6), 875-880
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Lung Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Secretory** leukoprotease inhibitor (SLPI) is a serine protease inhibitor involved in antineutrophil elastase protection at inflammatory sites. To elucidate both the function and regulation of SLPI in vivo, we isolated and characterized the mouse Slpi gene. An entire 3-kb mouse Slpi gene fragment was sequenced, including an 0.8-kb 5'-flanking region, the 2.2-kb Slpi gene, and a 0.1-kb 3'-flanking region. The mouse Slpi gene spans 2,222 base pairs containing four exons and three introns. All splicing borders between exons and introns are conserved as predicted by GT-AG rules. Using primer extension anal., the transcription start site was located 20 nucleotides upstream from the methionine (ATG) initiation codon. At the defined transcription start site, the sequence TCA+1GAGC is present. These results indicate that both mouse and human genomic structure are highly conserved. Using fluorescence in situ hybridization, we confirmed that, consistent with the genomic similarity, the **human** SLPI gene is localized on **chromosome** 20q12-**13**.2 and the mouse homolog on chromosome 2H, which are syntenic with each other.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 04 Feb 1998
ACCESSION NUMBER: 1998:62932 HCAPLUS
DOCUMENT NUMBER: 128:201577

TITLE: Cloning and characterization of two human G **protein**-coupled receptor genes (GPR38 and GPR39) related to the growth hormone **secretagogue** and neurotensin receptors

AUTHOR(S): McKee, Karen Kulji; Tan, Carina P.; Palyha, Oksana C.; Liu, Jim; Feighner, Scott D.; Hreniuk, Donna L.; Smith, Roy G.; Howard, Andrew D.; Van der Ploeg, Lex H. T.

CORPORATE SOURCE: Dep. of Biochemistry and Physiology, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Genomics (1997), 46(3), 426-434
CODEN: GNMCEP; ISSN: 0888-7543

PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The recent cloning of a growth hormone **secretagogue** receptor (GHS-R) from human pituitary gland and brain identified a third G **protein**-coupled receptor (GPC-R) involved in the control of growth hormone release. The nucleotide sequence of the GHS-R is most closely related to the neurotensin receptor-1 (NT-R1) (35% overall **protein** identity). Two human GPC-Rs related to both the type 1a GHS-R and NT-Rs were cloned and characterized. Hybridizations at low posthybridizational stringency with restriction enzyme-digested human genomic DNA resulted in the identification of a genomic clone encoding a first GHS-R/NT-R family member (GPR38). A cDNA clone was identified encoding a second GHS-R-related gene (GPR39). GPR38 and GPR39 share significant amino acid sequence identity with the GHS-R and NT-Rs 1 and 2. An acidic residue (E124) in TM-3, essential for the binding and activation of the GHS-R by structurally dissimilar GHSs, was conserved in GPR38 and GPR39. GPR38 is encoded by a single gene expressed in thyroid gland, stomach, and bone marrow. GPR39 is encoded by a highly conserved single-copy gene, expressed in brain and other peripheral tissues. Fluorescence in situ hybridization localized the genes for GPR38 and GPR39 to sep. chromosomes, distinct from the gene encoding the GH-R and NT-R type 1. The ligand-binding and functional properties of GPR38 and GPR39 remain to be determined

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 11 Jun 1996
ACCESSION NUMBER: 1996:337187 HCAPLUS
DOCUMENT NUMBER: 125:27353
TITLE: Tandem arrangement of the human serum albumin multigene family in the sub-centromeric region of 4q: evolution and chromosomal direction of transcription

AUTHOR(S): Nishio, Hitomi; Heiskanen, Mervi; Palotie, Aarno; Belanger, Luc; Dugaiczyk, Achilles

CORPORATE SOURCE: Department Biochemistry, University California, Riverside, CA, 92521, USA

SOURCE: Journal of Molecular Biology (1996), 259(1), 113-119
CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The albumin gene family is comprised of four genes encoding: serum albumin (ALB), α-fetoprotein (AFP), α-albumin (ALF), and vitamin D-binding **protein** (DBP; also known as GC). The genes are regulated developmentally, expressed in the liver, and the **proteins** are **secreted** into the bloodstream. The GC gene, and the tandemly linked ALB and AFP genes, have been previously localized to **human chromosome** 4q11-**13**. Using techniques of fluorescence in situ hybridization to chromatin fibers, chromosome walking and DNA sequencing of genomic clones, we now report on the chromosomal location of the ALF gene and the organization of the entire gene family. The four genes are tandemly linked in the 4q subcentromeric region: 5'ALB-5'AFP-5'ALF-5'GC3'-centromere, and hence are transcribed in the same, centromere-bound, direction. The linear arrangement of the 4 genes along the chromosome is not correlated with their temporal expression in the human ontogeny. It appears that GC is very close (and may be the gene proximal) to the centromere. The linear chromosomal arrangement of the four genes and the structural differences between them are congruent with the following evolutionary divergence of the gene family. Starting with the first duplication of an ancestral progenitor gene, a single evolutionary line led to the contemporary GC, leaving ALB/AFP/ALF on the other line of descent. The second duplication occurred in this ALB lineage, giving rise to ALB and the AFP/ALF progenitor, and the third, most recent one, gave rise to the AFP-ALF pair.

L7 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 Oct 1994
ACCESSION NUMBER: 1994:571807 HCAPLUS
DOCUMENT NUMBER: 121:171807
TITLE: βig-h3: a transforming growth factor-β-responsive gene encoding a **secreted protein** that inhibits cell attachment in vitro and suppresses the growth of CHO cells in nude mice
AUTHOR(S): Skonier, John; Bennett, Kelly; Rothwell, Victoria; Kosowski, Steve; Plowman, Greg; Wallace, Phil; Edelhoff, Susanne; Disteche, Christine; Neubauer, Mike; et al.
CORPORATE SOURCE: Pharmaceutical Research Institute, Bristol-Myers Squibb, Seattle, WA, 98121, USA
SOURCE: DNA and Cell Biology (1994), 13(6), 571-584
CODEN: DCEBE8; ISSN: 1044-5498
DOCUMENT TYPE: Journal
LANGUAGE: English
AB βIg-h3 is a novel gene first discovered by differential screening of a cDNA library made from A549 human lung adenocarcinoma cells treated with transforming growth factor-β1 (TGF-β1). It encodes a 683-amino-acid **protein** containing a **secretory** signal sequence and four homologous internal domains. Here the authors show that treatment of several types of cells, including human melanoma cells, human mammary epithelial cells, human keratinocytes, and human fibroblasts, with TGF-β

resulted in a significant increase in βig-h3 RNA. A portion of the βig-h3 coding sequence was expressed in bacteria, and antisera against the bacterially produced **protein** was raised in rabbits. This antisera was used to demonstrate that several cell lines **secreted** a 68-kD βIG-H3 **protein** after treatment with TGF-β. Transfection of βIG-H3 expression plasmids into Chinese hamster ovary (CHO) cells led to a marked decrease in the ability of these cells to form tumors in nude mice. The βIG-H3 **protein** was purified from media conditioned by recombinant CHO cells, characterized by immunoblotting and **protein** sequencing and shown to function in an anti-adhesion assay in that it inhibited the attachment of A549, HeLa, and WI-38 cells to plastic in serum-free media. Sequencing of cDNA clones encoding murine βig-H3 indicated 90.6% conservation at the amino acid level between the murine and human **proteins**. Finally, the βig-h3 gene was localized to human chromosome 5q31, a region frequently deleted in preleukemic myelodysplasia and leukemia. The corresponding mouse βig-h3 gene was mapped to mouse **chromosome 13** region B to C1, which confirms a region of conservation on **human** chromosome 5 and mouse **chromosome 13** . The authors suggest that this **protein** be named p68βig-h3.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:37:06 ON 28 APR 2004)

L8 47 S L7
L9 27 DUP REM L8 (20 DUPLICATES REMOVED)

L9 ANSWER 1 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-532906 [50] WPIDS
DOC. NO. CPI: C2003-144115
TITLE: Targeting a molecule to a leukemia cell, useful for treating leukemia, comprises contacting the cell with a retinoid to increase the expression of a marker in a cell, and contacting the cell with an agent that specifically binds the marker.
DERWENT CLASS: B04
INVENTOR(S): YANG, L; LIJUN, Y
PATENT ASSIGNEE(S): (YANG-I) YANG L; (UYFL) UNIV FLORIDA
COUNTRY COUNT: 100
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2003050257 | A2 | 20030619 | (200350)* | EN | 29 |
| RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW | | | | | |
| W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW | | | | | |
| US 2003124127 | A1 | 20030703 | (200351) | | |
| AU 2002360525 | A1 | 20030623 | (200420) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2003050257 | A2 | WO 2002-US39294 | 20021206 |
| US 2003124127 | A1 Provisional | US 2001-338373P | 20011206 |
| | | US 2002-313250 | 20021206 |
| AU 2002360525 | A1 | AU 2002-360525 | 20021206 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 2002360525 | A1 Based on | WO 2003050257 |

PRIORITY APPLN. INFO: US 2001-338373P 20011206; US 2002-313250 20021206

AN 2003-532906 [50] WPIDS

AB WO2003050257 A UPAB: 20030805

NOVELTY - Targeting a molecule to a leukemia cell comprising contacting the cell with a retinoid to increase the expression of a marker in a cell, and contacting the cell with an agent that specifically binds the marker, where the agent can be a molecule or a substance to which the molecule is attached, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for targeting a molecule to a leukemia cell, comprising a retinoid for increasing the expression of a marker in a cell, and an agent that specifically binds to the marker.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Immunotherapy.

USE - The method is useful for treating leukemia, particularly, acute promyelocytic leukemia (APL). The kit is useful for targeting a molecule to a leukemia cell (claimed).

Dwg.0/10

L9 ANSWER 2 OF 27 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2002661873 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12421943

TITLE: Dendritic cell-associated lectin-1: a novel dendritic cell-associated, C-type lectin-like molecule enhances T cell **secretion** of IL-4.

AUTHOR: Ryan Elizabeth J; Marshall Aaron J; Magaletti Dario; Floyd Helen; Draves Kevin E; Olson N Eric; Clark Edward A

CORPORATE SOURCE: Regional Primate Research Center, Box 357330, University of Washington, Seattle, WA 98195, USA.. ejryan@u.washington.edu

CONTRACT NUMBER: AI 44257 (NIAID)
DE 13061 (NIDCR)
GM 37905 (NIGMS)
RR 00166 (NCRR)

SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2002 Nov 15) 169 (10) 5638-48.
Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-AF518873
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021108
Last Updated on STN: 20030115
Entered Medline: 20030114

AB We have characterized dendritic cell (DC)-associated lectin-1 (DCAL-1), a novel, type II, transmembrane, C-type lectin-like **protein**. DCAL-1 has restricted expression in hemopoietic cells, in particular, DCs and B cells, but T cells and monocytes do not express it. The DCAL-1 locus is within a cluster of C-type lectin-like loci on **human chromosome** 12p12-**13** just 3' to the CD69 locus. The consensus sequence of the DCAL-1 gene was confirmed by RACE-PCR; however, based on sequence alignment with genomic DNA and with various human expressed sequence tags, we predict that DCAL-1 has two splice variants. C-type lectins share a common sequence motif of 14 invariable and 18 highly conserved aa residues known as the carbohydrate recognition domain. DCAL-1, however, is missing three of the cysteine residues required to form the standard carbohydrate recognition domain. DCAL-1 mRNA and **protein** expression are increased upon the differentiation of monocytes to CD1a(+) DCs. B cells also express high levels of DCAL-1 on their cell surface. Using a DCAL-1 fusion **protein** we identified a population of CD4(+) CD45RA(+) T cells that express DCAL-1 ligand. Coincubation with soluble DCAL-1 enhanced the proliferation of CD4(+) T cells in response to CD3 ligation and significantly increased IL-4 **secretion**. In contrast, coincubation with soluble DC-specific ICAM-3-grabbing nonintegrin (CD209) fusion **protein** as a control had no effect on CD4(+) T cell proliferation or IL-4 and IFN-gamma **secretion**. Therefore, the function of DCAL-1 on DCs and B cells may act as a T cell costimulatory molecule, which skews CD4(+) T cells toward a Th2 response by enhancing their **secretion** of IL-4.

L9 ANSWER 3 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:545409 SCISEARCH
THE GENUINE ARTICLE: 568BH
TITLE: Higher expression of human kallikrein 10 in breast cancer tissue predicts tamoxifen resistance
AUTHOR: Luo L Y; Diamandis E P; Look M P; Soosaipillai A P; Foekens J A (Reprint)
CORPORATE SOURCE: Rotterdam Canc Inst, Daniel Den Hoed Kliniek, Dept Med Oncol, Div Endocrine Oncol, Rotterdam, Netherlands (Reprint); Univ Rotterdam Hosp, Rotterdam, Netherlands; Mt Sinai Hosp, Dept Pathol & Lab Med, Toronto, ON M5G 1X5, Canada; Univ Toronto, Dept Lab Med & Pathobiol, Toronto, ON M5G 1L5, Canada
COUNTRY OF AUTHOR: Netherlands; Canada
SOURCE: BRITISH JOURNAL OF CANCER, (5 JUN 2002) Vol. 86, No. 11, pp. 1790-1796.
Publisher: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
ISSN: 0007-0920.

Searcher : Shears 571-272-2528

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The **human** tissue kallikreins are **secreted** serine proteases, encoded by a group of homologous genes clustered in tandem on **chromosome** 19q **13**.3-4, **Human** kallikrein 6 and **human** 1 10 are two new members of this family. Recently, we developed highly sensitive and specific immunofluorometric assays for **human** kallikrein 6 and **human** kallikrein 10, which allow for their quantification in tissue extracts and biological fluids. Both **human** kallikrein 6 and **human** kallikrein 10 are found to be down-regulated in breast cancer cell lines, suggesting that they may be involved in breast cancer pathogenesis and progression, in this study, we investigated the potential value of **human** kallikrein 6 and **human** kallikrein 10 as prognostic and predictive factors in breast cancer, We quantified **human** kallikrein 6 and **human** kallikrein 10 **protein** levels in 749 breast tumour cytosolic extracts and correlated this data with various clinicopathological variables and patient outcomes, **Human** kallikrein 6 and **human** kallikrein 10 are positively correlated with each other. Higher **human** Kallikrein 6 and **human** kallikrein. 0 **protein** levels are associated with younger age, pre-menopausal, status and tumours which are negative for oestrogen and progesterone receptors. No correlation was found between **human** kallikrein 6 and **human** kallikrein 10 levels and tumour size, grace, and nodal status, Survival analysis showed that neither **human** kallikrein 6 nor **human** kallikrein 10 are related to the rate of relapse-free and overall survival. In the analysis with respect to response to tamoxifen therapy, although **human** kallikrein 6 levels were not associated with tamoxifen responsiveness, higher levels of **human** kallikrein 10 were significantly associated with a poor response rate. This association remained significant in the multivariate analysis Further-more, higher **human** kallikrein 10 levels were significantly related with a short progression-free and post-relapse overall survival after start of tamoxifen treatment for advanced disease. Taken together, our results suggest that although **human** kallikrein 6 and **human** kallikrein 10 are not prognostic markers for breast cancer, **human** kallikrein 10 is an independent predictive marker for response of tamoxifen therapy.

L9 ANSWER 4 OF 27 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002657267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12206714
TITLE: A locus on human chromosome 20 contains several genes expressing protease inhibitor domains with homology to whey acidic **protein**.
AUTHOR: Clauss Adam; Lilja Hans; Lundwall Ake
CORPORATE SOURCE: Wallenberg Laboratory, Department of Laboratory Medicine, University Hospital MAS, Lund University, S-205 02 Malmo, Sweden.
SOURCE: Biochemical journal, (2002 Nov 15) 368 (Pt 1) 233-42.

Searcher : Shears 571-272-2528

Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF454505; GENBANK-AF454506; GENBANK-AF454507; GENBANK-AF488306; GENBANK-AF492015; GENBANK-AF492016; GENBANK-AY038181; GENBANK-AY038182; GENBANK-AY047609; GENBANK-AY047610
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021106
Last Updated on STN: 20021228
Entered Medline: 20021227

AB A locus containing 14 genes, encoding **protein** domains that have homology with whey acidic **protein** (WAP), has been identified in a region of 678 kb on **human chromosome** 20q12-**13**.1. Among them are genes of the known or postulated protease inhibitors elafin, **secretory** leucocyte protease inhibitor, human epididymis gene product 4, eppin, and huWAP2. Nucleotide sequences of full-length transcripts were obtained from cDNA fragments generated by rapid amplification of cDNA ends. Characteristic features of the genes are that the upstream promoter regions are devoid of TATA-boxes and that the coding nucleotides are divided into distinct exons for the signal **peptide** and for each WAP domain. In most cases, there is also a separate exon encompassing a few terminal codons and the 3' untranslated nucleotides. There are also examples of mixed type inhibitors, that encode inhibitor domains of both WAP and Kunitz types. Several of the genes appear to be expressed ubiquitously, but, in most cases, the highest transcript levels are found in epididymis followed by testis and trachea. Some of the genes also display high transcript levels in neural tissues. Potential biological roles of **protein** products could be in host defence against invading micro-organisms or in the regulation of endogenous proteolytic enzymes, of which those originating from the kallikrein gene locus on chromosome 19 are of particular interest.

L9 ANSWER 5 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 3
ACCESSION NUMBER: 2002034207 EMBASE
TITLE: Identification and characterization of a novel family of mammalian ependymin-related **proteins** (MERPs) in hematopoietic, nonhematopoietic, and malignant tissues.
AUTHOR: Apostolopoulos J.; Sparrow R.L.; McLeod J.L.; Collier F.M.; Darcy P.K.; Slater H.R.; Ngu C.; Gregorio-King C.C.; Kirkland M.A.
CORPORATE SOURCE: Dr. J. Apostolopoulos, Research Unit, Aust. Red Cross Blood Serv.-Victoria, Kavanagh and Balston Streets, Southbank, Vic. 3006, Australia.
japostolopoulos@arcbs.redcross.org.au
SOURCE: DNA and Cell Biology, (2001) 20/10 (625-635).
Refs: 24
ISSN: 1044-5498 CODEN: DCEBE8
COUNTRY: United States

Searcher : Shears 571-272-2528

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Evidence is presented for a family of mammalian homologs of ependymin, which we have termed the mammalian ependymin-related **proteins** (MERPs). Ependymins are **secreted** glycoproteins that form the major component of the cerebrospinal fluid in many teleost fish. We have cloned the entire coding region of **human** MERP-1 and mapped the gene to chromosome 7p14.1 by fluorescence in situ hybridization. In addition, three **human** MERP pseudogenes were identified on chromosomes 8, 16, and X. We have also cloned the mouse MERP-1 homolog and an additional family member, mouse MERP-2. Then, using bioinformatics, the mouse MERP-2 gene was localized to **chromosome 13**, and we identified the monkey MERP-1 homolog and frog ependymin-related **protein** (ERP). Despite relatively low amino acid sequence conservation between piscine ependymins, toad ERP, and MERPs, several amino acids (including four key cysteine residues) are strictly conserved, and the hydropathy profiles are remarkably alike, suggesting the possibilities of similar **protein** conformation and function. As with fish ependymins, frog ERP and MERPs contain a signal **peptide** typical of **secreted proteins**. The MERPs were found to be expressed at high levels in several hematopoietic cell lines and in nonhematopoietic tissues such as brain, heart, and skeletal muscle, as well as several malignant tissues and malignant cell lines. These findings suggest that MERPs have several potential roles in a range of cells and tissues.

L9 ANSWER 6 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:337054 SCISEARCH
THE GENUINE ARTICLE: 424FR
TITLE: Sequence, genomic structure and tissue expression of Human BRI3, a member of the BRI gene family
AUTHOR: Vidal R (Reprint); Calero M; Revesz T; Plant G; Ghiso J; Frangione B
CORPORATE SOURCE: Indiana Univ, Sch Med, Dept Pathol & Lab Med, 636 Barnhill Dr, MS A133, Indianapolis, IN 46202 USA (Reprint); NYU, Sch Med, Dept Pathol, New York, NY USA; Inst Neurol, Dept Neuropathol, London, England; Natl Hosp Neurol & Neurosurg, London, England
COUNTRY OF AUTHOR: USA; England
SOURCE: GENE, (21 MAR 2001) Vol. 266, No. 1-2, pp. 95-102. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0378-1119.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 35

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The BRI3 gene is a member of the BRI gene family, made up of at least three different genes (BRI1-3) Previous studies established the cDNA sequence and structure of the **human** and mouse BRI1 and BRI2 genes and we recently reported that mutations in the BRI2 isoform, located on **chromosome 13**, are

associated with dementia in **humans**. In the present work. we determine the complete cDNA sequence and genomic organization of the **human** BRI3 gene. BRI3 codes for a **polypeptide** of 267 amino acids, with a Mr of 30 KDa and a pi of 8.47. The amino acid sequence is 43.7% identical to the sequence of the **human** BRI2, and 38.3% identical to that of **human** BRII, with the highest percentage of amino acid identity bring concentrated on the C-terminal half of the molecules. In Northern blots, BRI3 cDNA hybridizes only one message of approximately 2.1 kilobases, which is predominantly present in the **human** brain. The BRI3 gene is localized on chromosome 2 and consists of six exons spanning more than 20 kb. Homology search of EST data banks retrieved a Caenorhubditis briggsae homolog of BRI, indicating that the BRI gene belongs to a strongly conserved gene family. These studies, aimed at characterizing the members of the BRI gene family, may provide valuable clues to the understanding of their normal function and how mutations in BRII can cause neurodegeneration and dementia similar to Alzheimer's disease. (C) 2001 Elsevier Science B.V. All rights reserved.

L9 ANSWER 7 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-387729 [33] WPIDS
DOC. NO. NON-CPI: N2000-290256
DOC. NO. CPI: C2000-117734
TITLE: Novel human **secreted proteins** useful for diagnosing, preventing, treating and ameliorating a medical condition e.g. cardiovascular disease.
DERWENT CLASS: B04 C06 D13 D16 S03
INVENTOR(S): BIRSE, C E; CARTER, K C; EBNER, R; FLORENCE, K A; KOMATSOULIS, G; NI, J; ROSEN, C A; RUBEN, S M; YOUNG, P E
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC; (BIRS-I) BIRSE C E; (CART-I) CARTER K C; (EBNE-I) EBNER R; (FLOR-I) FLORENCE K A; (KOMA-I) KOMATSOULIS G; (NIJJ-I) NI J; (ROSE-I) ROSEN C A; (RUBE-I) RUBEN S M; (YOUN-I) YOUNG P E
COUNTRY COUNT: 88
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2000029422 | A1 | 20000525 | (200033)* | EN | 295 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2000017162 | A | 20000605 | (200042) | | |
| EP 1137656 | A1 | 20011004 | (200158) | EN | |
| R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI | | | | | |
| JP 2002530058 | W | 20020917 | (200276) | | 430 |
| US 2003050460 | A1 | 20030313 | (200321) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| WO 2000029422 | A1 | | WO 1999-US26409 | 19991109 |
| AU 2000017162 | A | | AU 2000-17162 | 19991109 |
| EP 1137656 | A1 | | EP 1999-960249 | 19991109 |
| | | | WO 1999-US26409 | 19991109 |
| JP 2002530058 | W | | WO 1999-US26409 | 19991109 |
| | | | JP 2000-582409 | 19991109 |
| US 2003050460 | A1 | Provisional | US 1998-108207P | 19981112 |
| | | CIP of | WO 1999-US26409 | 19991109 |
| | | Cont of | US 2000-565391 | 20000505 |
| | | | US 2001-948820 | 20010910 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 2000017162 | A | Based on | WO 2000029422 |
| EP 1137656 | A1 | Based on | WO 2000029422 |
| JP 2002530058 | W | Based on | WO 2000029422 |

PRIORITY APPLN. INFO: US 1998-108207P 19981112; US 2000-565391 20000505; US 2001-948820 20010910

AN 2000-387729 [33] WPIDS

AB WO 200029422 A UPAB: 20000712

NOVELTY - Human **secreted** polynucleotides and the **proteins** they encode are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) an isolated nucleic acid molecule (I) comprising a polynucleotide with a nucleotide sequence at least 95% identical to one of the following sequences:

(a) a polynucleotide fragment of one of 31 defined gene sequences (A) given in the specification or a polynucleotide fragment of the cDNA sequence included in one of 31 ATCC deposits (C) which is hybridizable to (A);

(b) a polynucleotide encoding a **polypeptide** fragment of one of 31 defined sequences (B) given in the specification or a polynucleotide fragment of (C);

(c) a polynucleotide encoding a **polypeptide** domain of (B) or a **polypeptide** domain encoded by (C);

(d) a polynucleotide encoding a **polypeptide** epitope of (B) or a **polypeptide** epitope encoded by (C);

(e) a polynucleotide encoding a **polypeptide** of (B) or the cDNA sequence included in (C), having biological activity;

(f) a polynucleotide which is a variant of (A);

(g) a polynucleotide which is an allelic variant of (A);

(h) a polynucleotide which encodes a species homologue of (B); or

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides of (a)-(h) but does not hybridize to a nucleic acid molecule with a nucleotide sequence of only A or T residues;

(2) a recombinant vector comprising (I);

(3) a method of preparing a recombinant host cell comprising (I);

(4) a recombinant host cell produced by the method of (3);

(5) an isolated **polypeptide** (II) comprising an amino acid sequence at least 95% identical to one of the following sequences:

(a) a **polypeptide** fragment of (B) or the encoded sequence included in (C);

(b) a **polypeptide** fragment of (B) or the encoded sequence included in (C) with biological activity;

(c) a **polypeptide** epitope of (B) or the encoded sequence included in (C);

(d) a **secreted** form of (B) or the encoded sequence included in (C);

(e) a full length **protein** of (B) or the encoded sequence included in (C);

(f) a variant of (B);

(g) an allelic variant of (B); or

(h) a species homologue of (B);

(6) an isolated antibody that binds specifically to (II);

(7) a recombinant host cell that expresses (II);

(8) a method of making (II) comprising culturing the recombinant host cell of (7) under conditions so that the **polypeptide** is expressed and recovering the **polypeptide**;

(9) a method for diagnosing a pathological condition or susceptibility to a pathological condition in a subject comprising determining the presence or absence of a mutation in (I) and making a diagnosis based on the presence or absence of the mutation;

(10) a method for diagnosing a pathological condition or susceptibility to a pathological condition in a subject comprising determining the presence or amount of expression of (II) in a biological sample and making a diagnosis based on the presence or amount of expression of the **protein**;

(11) a method of identifying a binding partner to (II) comprising contacting (II) with a binding partner and determining any effect on the activity of (II);

(12) the gene corresponding to the cDNA sequence of (C);

(13) a method of identifying an activity in a biological assay comprising expressing (A) in a host cell, isolating the supernatant, detecting an activity in a biological assay and identifying the protein in the supernatant with the activity; and

(14) the product identified by the method of (13).

ACTIVITY - Cytostatic; proliferative; antiallergic, dermatological; immunosuppressive; antiarrhythmic; cardiant; vulnerary; antibacterial; virucide.

Human umbilical vein endothelial cells (HUVEC) were seeded at 2-5 x 104 cells/35 mm dish density in M199 medium containing 4% fetal bovine serum (FBS), 16 units/ml heparin and 50 units/ml endothelial cell growth supplements. The following day the medium was replaced with M199 containing 10% FBS and 8 units/ml heparin. A polypeptide with amino acid sequence (B) and positive controls e.g. basic fibroblast growth factor (bFGF) were added at various concentrations. The medium was replaced on days 4 and 6 and on day 8 cell number was determined with a Coulter counter. An increase in

the number of HUVEC cells would indicate the polypeptide of the invention proliferates vascular endothelial cells. No results are given.

MECHANISM OF ACTION - Gene therapy.

USE - (I) and (II) are used for preventing, treating or ameliorating a medical condition and for diagnosing a pathological condition or susceptibility to a condition in a subject (all claimed). Conditions which can be detected and treated include cancer and other proliferative cell disorders, disorders of the immune system e.g. systemic lupus erythemoatosus and allergic reactions, cardiovascular disorders e.g. cardiac arrest and arrhythmia, wound healing, cell regeneration and viral and bacterial infections. Subjects which may be treated include humans, rabbits, goats, cows, mice, dogs or cats.

(I) can be used as a chromosome marker e.g. for forensic biology and in gene therapy. (II) and antibodies to (II) can be used to assay protein levels in a biological sample to allow detection of a disease before clinical symptoms appear and to treat disease.

(I) and (II) may also be used as food additives or preservatives to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals or other nutritional components.

**Dwg.0/0**

L9 ANSWER 8 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-195448 [17] WPIDS
DOC. NO. NON-CPI: N2000-144569
DOC. NO. CPI: C2000-060674
TITLE: Isolated beta IV spectrin **polypeptides** which interact with autoantigens and modulate hormone and neuropeptide **secretion**, used for developing products for the diagnosis and treatment of autoimmune disease such as type I diabetes.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BERGHS, C A F M; DIRKX, R A; SOLIMENA, M
PATENT ASSIGNEE(S): (UYYA) UNIV YALE
COUNTRY COUNT: 87
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2000007610 | A1 | 20000217 | (200017)* | EN | 98 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW | | | | | |
| AU 9954696 | A | 20000228 | (200030) | | |
| US 6187563 | B1 | 20010213 | (200111) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|

| | | | |
|---|---|---|---|
| WO 2000007610 | A1 | WO 1999-US17916 | 19990806 |
| AU 9954696 | A | AU 1999-54696 | 19990806 |
| US 6187563 | B1 Provisional | US 1998-95657P | 19980807 |
| | | US 1999-368590 | 19990804 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 9954696 | A Based on | WO 2000007610 |

PRIORITY APPLN. INFO: US 1999-368590 19990804; US 1998-95657P 19980807

AN 2000-195448 [17] WPIDS

AB WO 200007610 A UPAB: 20000706

NOVELTY - An isolated **polypeptide** (I) or fragment, termed beta IV spectrin is characterized by a defined **polypeptide** sequence (II) of 2293 amino acids given in the specification, or a fragment of (II).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an isolated nucleic acid which encodes (I);

(2) a method of identifying the presence of type I diabetes in a patient comprising contacting the body fluid from the patient with (I) to form a complex and detecting the presence or absence of the complex;

(3) an isolated **polypeptide** or fragment which interacts with an autoantigen of type I diabetes, the isolated **polypeptide** or fragment being a member of the spectrin family; and

(4) an isolated nucleic acid which codes for a **polypeptide** or fragment which interacts with an autoantigen of type I diabetes, the nucleic acid or fragment being a member of the spectrin family.

ACTIVITY - Antidiabetic; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Interactor of type I diabetes autoantigens, ICA512 and phogrin.

USE - The **polypeptides** or fragments can be used for modulating neuropeptide or hormone release in a patient (claimed). The products can be used to attenuate, inhibit, or prevent the destruction of pancreatic beta -cells associated with the onset of insulin-dependent diabetes mellitus. (I) can be used for identifying individuals who suffer from or are susceptible to type I diabetes (claimed). The assays will also be useful for monitoring the effect of immunotherapy to block or prevent autoimmune reactions to the beta -cell and for monitoring the progress of the disease from pre-diabetes to clinical diabetes and will be particularly useful for monitoring the status of transplanted pancreatic beta -cells in diabetic patients who have undergone an islet cell graft.

Dwg.0/10

L9 ANSWER 9 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:918364 SCISEARCH
THE GENUINE ARTICLE: 378MN
TITLE: beta IV spectrin, a new spectrin localized at axon

initial segments and nodes of ranvier in the central and peripheral nervous system

AUTHOR: Berghs S; Aggujaro D; Dirkx R; Maksimova E; Stabach P; Hermel J M; Zhang J P; Philbrick W; Slepnev V; Ort T; Solimena M (Reprint)

CORPORATE SOURCE: YALE UNIV, SCH MED, DEPT INTERNAL MED, ENDOCRINOL SECT, 330 CEDAR ST, NEW HAVEN, CT 06520 (Reprint); YALE UNIV, SCH MED, DEPT INTERNAL MED, ENDOCRINOL SECT, NEW HAVEN, CT 06510; YALE UNIV, SCH MED, DEPT CELL BIOL, NEW HAVEN, CT 06510; YALE UNIV, SCH MED, DEPT PATHOL, NEW HAVEN, CT 06510

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF CELL BIOLOGY, (27 NOV 2000) Vol. 151, No. 5, pp. 985-1001.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021.
ISSN: 0021-9525.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 84

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB We report the identification of beta IV spectrin, a novel spectrin isolated as an interactor of the receptor tyrosine phosphatase-like **protein** ICA512, The beta IV spectrin gene is located on **human** and mouse **chromosomes** 19q13. **13** and 7b2, respectively. Alternative splicing of beta IV spectrin generates at least four distinct isoforms, numbered beta IV Sigma1-beta IV Sigma4 spectrin. The longest isoform (beta IV Sigma1 spectrin) includes an actin-binding domain, followed by 17 spectrin repeats, a specific domain in which the amino acid sequence ERQES is repeated four times, several putative SH3-binding sites and a pleckstrin homology domain. beta IV Sigma2 and beta IV Sigma3 spectrin encompass the NH2- and COOH-terminal halves of beta IV Sigma1 spectrin, respectively, while beta IV Sigma4 spectrin lacks the ERQES and the pleckstrin homology domain. Northern blots revealed an abundant expression of PIV spectrin transcripts in brain and pancreatic islets, By immunoblotting, beta IV Sigma1 spectrin is recognized as a **protein** of 250 kD. Anti-beta IV spectrin antibodies also react with two additional isoforms of 160 and 140 kD. These isoforms differ from beta IV Sigma1 spectrin in terms of their distribution on subcellular fractionation, detergent extractability, and phosphorylation. In islets, the immunoreactivity for beta IV spectrin is more prominent in alpha than in beta cells. In brain, beta IV spectrin is enriched in myelinated neurons, where it colocalizes with ankyrin(G) 480/270-kD at axon initial segments and nodes of Ranvier. Likewise, beta IV spectrin is concentrated at the nodes of Ranvier in the rat sciatic nerve. In the rat hippocampus, beta IV Sigma1 spectrin is detectable from embryonic day 19, concomitantly with the appearance of immunoreactivity at the initial segments. Thus, we suggest that beta IV Sigma1 spectrin interacts with ankyrin, 480/270-kD and participates in the clustering of voltage-gated Na+ channels and cell-adhesion molecules at initial segments and nodes of Ranvier.

L9 ANSWER 10 OF 27 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2000487492 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11037750
TITLE: Enamelin maps to human chromosome 4q21 within the autosomal dominant amelogenesis imperfecta locus.
AUTHOR: Dong J; Gu T T; Simmons D; MacDougall M
CORPORATE SOURCE: Department of Pediatric Dentistry, Dental School, University of Texas Health Science Center at San Antonio, 78229-3900, USA.
CONTRACT NUMBER: P01 DE13221 (NIDCR)
R01 DE09875 (NIDCR)
SOURCE: European journal of oral sciences, (2000 Oct) 108 (5) 353-8.
Journal code: 9504563. ISSN: 0909-8836.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010125

AB Amelogenesis imperfecta is a group of hereditary enamel defects. Of the autosomal dominant forms, only the local hypoplastic type has been mapped to **human chromosome** 4q **13** -4q21. Enamelin is a large enamel matrix **protein secreted** by ameloblasts. The purpose of this study was to determine the human chromosomal localization of enamelin to establish an association with various forms of amelogenesis imperfecta. Chromosomal mapping was performed by polymerase chain reaction (PCR) amplification using somatic hybrid and deletion/derivation cell line panels with an enamelin primer set based on 100% conserved regions between pig and mouse cDNAs. Sequence-tagged site content mapping using eight markers within the critical local hypoplastic amelogenesis imperfecta region was then performed using an isolated human enamelin genomic BAC clone. The human enamelin amplicon was confirmed by DNA sequence analysis, revealing 81% and 73% identity to pig and mouse cDNAs, respectively. PCR amplification using a somatic cell hybrid panel placed enamelin on chromosome 4 with analysis of a regional chromosome 4 mapping panel refining the localization to 4q 13.1-q21.23. An identified human enamelin BAC genomic clone was shown to contain markers D4S2604 and D4S2670, as well as the first exon of the human ameloblastin gene, placing enamelin in the critical amelogenesis imperfecta locus between markers HIS1 and D4S2604 at 4q21. Our results suggest that enamelin is a strong candidate gene for this disease. Furthermore, human 4q21 may contain a second cluster of enamel matrix genes located proximally to the identified cluster of dentin and bone genes.

L9 ANSWER 11 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-116550 [10] WPIDS
DOC. NO. CPI: C2000-035630
TITLE: New mammalian corin for treatment or diagnosis of, e.g. cardiac and kidney disease.
DERWENT CLASS: B04 D16
INVENTOR(S): MORSER, M J; WU, Q; YAN, W

PATENT ASSIGNEE(S): (SCHD) SCHERING AG
COUNTRY COUNT: 87
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9964608 | A1 | 19991216 | (200010)* | EN | 64 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW | | | | | |
| AU 9945077 | A | 19991230 | (200022) | | |
| NO 2000006159 | A | 20010205 | (200115) | | |
| EP 1084259 | A1 | 20010321 | (200117) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |
| HU 2001002811 | A2 | 20011228 | (200216) | | |
| ZA 2000005483 | A | 20020130 | (200217) | | 77 |
| JP 2002517253 | W | 20020618 | (200242) | | 90 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9964608 | A1 | WO 1999-EP3895 | 19990604 |
| AU 9945077 | A | AU 1999-45077 | 19990604 |
| NO 2000006159 | A | WO 1999-EP3895 | 19990604 |
| | | NO 2000-6159 | 20001204 |
| EP 1084259 | A1 | EP 1999-927888 | 19990604 |
| | | WO 1999-EP3895 | 19990604 |
| HU 2001002811 | A2 | WO 1999-EP3895 | 19990604 |
| | | HU 2001-2811 | 19990604 |
| ZA 2000005483 | A | ZA 2000-5483 | 20001006 |
| JP 2002517253 | W | WO 1999-EP3895 | 19990604 |
| | | JP 2000-553598 | 19990604 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 9945077 | A | Based on | WO 9964608 |
| EP 1084259 | A1 | Based on | WO 9964608 |
| HU 2001002811 | A2 | Based on | WO 9964608 |
| JP 2002517253 | W | Based on | WO 9964608 |

PRIORITY APPLN. INFO: US 1999-314967 19990520; US 1998-92029 19980605

AN 2000-116550 [10] WPIDS

AB WO 9964608 A UPAB: 20000228
NOVELTY - Isolated, full-length mammalian corin **polypeptide** (I), or its biologically active fragments, excluding those encoded by Hs. 62794 (1686098, 1686206, 2537780, 1524579, 1881137 or 1524691) or Hs.71798 (1716421) with numbers referring to the PubEST database are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for

the following:
(1) isolated nucleic acid (II) encoding (I) and optionally present in a cloning vector;
(2) fragments (IIa) containing a contiguous segment of 12-100 bp, or its complement, from (II), optionally labeled and optionally with 1-5 nucleotide substitutions provided that it still hybridizes under stringent conditions to (II);
(3) recombinant production of human corin (Ia) by culturing cells transformed with (II);
(4) isolated (Ia) produced this way;
(5) vector containing (II);
(6) transformed host cells containing (II);
(7) identifying modulators of the serine protease activity of (I), and
(8) isolated antibodies (Ab) specific for human or murine corin.
ACTIVITY - Antihypertensive; anti-arrhythmic.
MECHANISM OF ACTION - (I) is a serine protease that cleaves atrial natriuretic **peptide** (ANP) (involved in e.g. body fluid homeostasis, blood pressure, vasodilation, natriuresis, inhibition of sodium absorption or aldosterone production/ **secretion**, glomerular filtration, mitogenesis), also it may be involved in diseases associated with cartilage-derived and cardiac cells, in heart disease, cell signaling, differentiation (of bone and/or cardiac cells) and processing of growth factors.
USE - (I) are used:
(a) to raise specific antibodies (Ab);
(b) as size markers, and
(c) to identify specific binding agents (potential therapeutic modulators).
Ab are used to detect/quantify (I), e.g. for diagnosis of diseases associated with atrial natriuretic **peptide** (ANP) such as congestive heart failure, cardiac arrhythmia and hemodynamic compromise, also as therapeutic agents, in research and for affinity purification of (I). Nucleic acid (II) that encodes (I) is used:
(i) for recombinant production of (I);
(ii) as source of oligonucleotide probes and primers for detecting or quantifying (I) (in research, diagnosis or forensics);
(iii) as antisense sequences for regulating expression of corin, and
(iv) as a marker (of size or in pedigree or disease mapping, e.g. of the ANP-related diseases listed above, also familial hypertrophic cardiomyopathy, osteoporosis, osteopetrosis, total anomalous pulmonary venous return).
Agents that modulate activity of (I), e.g. antisense sequences, ribozymes, enzyme inhibitors or (I)-expressing genes, are used for treatment of the specified disorders.
Dwg.0/0

L9 ANSWER 12 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-142930 [12] WPIDS
DOC. NO. CPI: C1999-041859
TITLE: New **secreted polypeptide**, zsig46, and its fragments, related fusion **proteins** - used for diagnosis and treatment of thyroid disorders or diseases involving genes on

chromosome 13.

DERWENT CLASS: B04 D16
INVENTOR(S): GILBERTSON, D G; SHEPPARD, P O
PATENT ASSIGNEE(S): (ZYMO) ZYMOGENETICS INC; (ZYMO) ZYMOGENETICS; (GILB-I) GILBERTSON D G; (SHEP-I) SHEPPARD P O
COUNTRY COUNT: 83
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9905275 | A1 | 19990204 | (199912)* | EN | 101 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW | | | | | |
| W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW | | | | | |
| AU 9885898 | A | 19990216 | (199926) | | |
| EP 1002077 | A1 | 20000524 | (200030) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |
| JP 2001511345 | W | 20010814 | (200154) | | 100 |
| US 2002042093 | A1 | 20020411 | (200227) | | |
| US 2002173624 | A1 | 20021121 | (200279) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| WO 9905275 | A1 | | WO 1998-US15431 | 19980724 |
| AU 9885898 | A | | AU 1998-85898 | 19980724 |
| EP 1002077 | A1 | | EP 1998-937110 | 19980724 |
| | | | WO 1998-US15431 | 19980724 |
| JP 2001511345 | W | | WO 1998-US15431 | 19980724 |
| | | | JP 2000-504249 | 19980724 |
| US 2002042093 | A1 | Provisional | US 1997-53613P | 19970724 |
| | | | US 1998-122383 | 19980724 |
| US 2002173624 | A1 | Provisional | US 1997-53613P | 19970724 |
| | | Cont of | US 1998-122383 | 19980724 |
| | | | US 2001-10050 | 20011109 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 9885898 | A | Based on | WO 9905275 |
| EP 1002077 | A1 | Based on | WO 9905275 |
| JP 2001511345 | W | Based on | WO 9905275 |

PRIORITY APPLN. INFO: US 1997-53613P 19970724; US 1998-122383 19980724; US 2001-10050 20011109

AN 1999-142930 [12] WPIDS
AB WO 9905275 A UPAB: 19990324
Isolated **polypeptide** (I) is at least 80% identical with the sequence of amino acids (aa) 31-346 of a 346 aa sequence (2) is given in the specification, and has Cys residues at the positions

corresponding to positions 58, 65, 132, 147, 153 and 219 of (2).

Also new are: (A) isolated **polypeptides** (II) comprising aa 1-37, 29-37, 31-37, 29-45, 31-45, 40-45, 40-346, 48-346, 29-276, 31-276, 40-276, 48-276 or 278-346 of (2), or their homologues with at least 80% identity; (B) fusion **protein** (FP1) comprising (i) any of (II), or the 1-346, 29-346 or 31-346 regions of (2) plus (ii) a second **polypeptide** (III); (C) fusion **proteins** (FP2) comprising aa 1-28 or 1-30 of (2) as **secretion** signal linked to (III); (D) **protein** (IV) comprising aa 1-29, 1-30, 48-276 or 31-346 of (2) complexed to (III); (E) expression vector containing a promoter and DNA encoding (I); (F) cells containing this vector; (G) antibody (Ab) or other binding **proteins** that bind to an epitope of (I); (H) isolated nucleic acid (V) encoding (I) (1486 bp sequence reproduced) or its nucleotide (nt) fragments 47-157, 131-157, 137-157, 131-181, 137-181, 164-1084, 164-181, 131-874, 137-874, 164-874, 188-874 or 878-1084, or their complements or degenerate forms; (J) isolated nucleic acids (Va) encoding FP1 or FP2; (K) isolated nucleic acid (VI) comprising a 1038 bp sequence (13), reproduced; and (L) oligonucleotide probes or primers containing at least 14 consecutive nt from (13) and their complements.

USE - Cells of (F) are used (a) to express (I) and (b) to screen for specific (ant)agonists. (I) is a **secreted protein**, designated zsig46, encoded by a gene on **human chromosome 13** and is mainly expressed in the thyroid. (I), either mature or including the signal sequence, and its fusions, can be used to study **secretion** of **proteins** from cells also to treat or prevent deficient expression of zsig46, which may be associated with thyroid diseases (e.g. hypothyroidism, Graves' disease, thyrotoxicosis, thyroid cancer etc.) or with diseases that involve genes in the same region of **chromosome 13** (e.g. Hirschsprung's disease, neuronal ceroid-lipofucinosis, Wilson disease and Reiger syndrome).

Other uses for (I) are to identify and isolate specific receptors or binding **proteins** and to raise Ab. (V), or its fragments, are used as hybridisation probes to detect genetic alterations, to generate transgenic animals, and to detect related sequences. While (IV) are used in gene or cellular therapy, and antisense sequences can be used to inhibit gene expression in vivo or in vitro.

Ab, and other binding **proteins**, are used as immunoassay reagents to detect zsig46 or cells expressing it, e.g. for assessing thyroid function to produce anti-idiotypic antibodies, for affinity purification of zsig46, to screen expression libraries, to neutralise zsig46 activity, and to deliver toxins, radioisotopes etc. for therapeutic or diagnostic purposes.

Agonists of (I) can be used to promote growth, differentiation and proliferation of specific cell types, e.g. for treating (extra)thyroid diseases or as additive to cell cultures.

Dwg.0/0

L9 ANSWER 13 OF 27 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1999133715 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9950216
TITLE: Netrin-1: interaction with deleted in colorectal cancer (DCC) and alterations in brain tumors and

neuroblastomas.

AUTHOR: Meyerhardt J A; Caca K; Eckstrand B C; Hu G; Lengauer C; Banavali S; Look A T; Fearon E R

CORPORATE SOURCE: Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor 48109-0638, USA.

CONTRACT NUMBER: CA21765 (NCI)
CA70097 (NCI)
CA71907 (NCI)

SOURCE: Cell growth & differentiation : molecular biology journal of the American Association for Cancer Research, (1999 Jan) 10 (1) 35-42.
Journal code: 9100024. ISSN: 1044-9523.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413

AB Netrins, a family of laminin-related **secreted proteins**, have critical roles in axon guidance and cell migration during development. The deleted in colorectal cancer (DCC) **protein** has been implicated as a netrin-1 receptor component. The expression and function of netrins in adult tissues remain unknown, and direct interaction of netrin-1 with DCC has not been demonstrated. We cloned the **human** netrin-1 (NTN1L) gene, mapped it to **chromosome** 17p12-**13**, and found that it encodes a 604 amino acid **protein** with 98% identity to mouse netrin-1 and 50% identity with the Caenorhabditis elegans UNC-6 **protein**. NTN1L transcripts were detected in essentially all normal adult tissues studied, and markedly reduced or absent NTN1L expression was seen in approximately 50% of brain tumors and neuroblastomas. In one neuroblastoma, missense mutations at highly conserved NTN1L codons were found. Netrin-1 **protein** could be cross-linked to DCC **protein** on the cell surface, but it did not immunoprecipitate with DCC in the absence of cross-linking and it failed to bind to a soluble fusion **protein** containing the entire DCC extracellular domain. Our findings demonstrating NTN1L loss of expression and mutations suggest that NTN1L alterations may contribute to the development of some cancers. Furthermore, the binding of netrin-1 to DCC appears to depend on the presence of a coreceptor or accessory **proteins**.

L9 ANSWER 14 OF 27 MEDLINE on STN

ACCESSION NUMBER: 1999061820 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9843921

TITLE: Structure of the murine **secretory** leukoprotease inhibitor (Slpi) gene and chromosomal localization of the human and murine SLPI genes.

AUTHOR: Kikuchi T; Abe T; Hoshi S; Matsubara N; Tominaga Y; Satoh K; Nukiwa T

CORPORATE SOURCE: Department of Respiratory Oncology and Molecular Medicine, Division of Cancer Control, Institute of Development, Aging and Cancer, Tohoku University,

Sendai, Japan.
SOURCE: American journal of respiratory cell and molecular biology, (1998 Dec) 19 (6) 875-80.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF002719; GENBANK-AF002720
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990119

AB **Secretory** leukoprotease inhibitor (SLPI) is a serine protease inhibitor involved in antineutrophil elastase protection at inflammatory sites. To elucidate both the function and regulation of SLPI in vivo, we isolated and characterized the mouse Slpi gene. An entire 3-kb mouse Slpi gene fragment was sequenced, including an 0. 8-kb 5'-flanking region, the 2.2-kb Slpi gene, and a 0.1-kb 3'-flanking region. The mouse Slpi gene spans 2,222 base pairs containing four exons and three introns. All splicing borders between exons and introns are conserved as predicted by GT-AG rules. Using primer extension analysis, the transcription start site was located 20 nucleotides upstream from the methionine (ATG) initiation codon. At the defined transcription start site, the sequence TCA+1GAGC is present. These results indicate that both mouse and human genomic structure are highly conserved. Using fluorescence in situ hybridization, we confirmed that, consistent with the genomic similarity, the **human** SLPI gene is localized on **chromosome** 20q12-**13**. 2 and the mouse homologue on chromosome 2H, which are syntenic with each other.

L9 ANSWER 15 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:673058 SCISEARCH
THE GENUINE ARTICLE: 115FY
TITLE: Mouse glycosylphosphatidylinositol-specific phospholipase D (Gpld1) characterization
AUTHOR: LeBoeuf R C (Reprint); Caldwell M; Guo Y; Metz C; Davitz M A; Olson L K; Deeg M A
CORPORATE SOURCE: UNIV WASHINGTON, DEPT MED, BOX 353410, SEATTLE, WA 98195 (Reprint); UNIV WASHINGTON, DEPT NUTR SCI, SEATTLE, WA 98195; NYU, SCH MED, DEPT PATHOL, NEW YORK, NY 10016; NYU, SCH MED, DEPT ENVIRONM MED, NEW YORK, NY 10016; MICHIGAN STATE UNIV, DEPT PHYSIOL, E LANSING, MI 48824; INDIANA UNIV, DEPT MED, INDIANAPOLIS, IN 46202; RICHARD L ROUDEBUSH VET AFFAIRS MED CTR, INDIANAPOLIS, IN 46202
COUNTRY OF AUTHOR: USA
SOURCE: MAMMALIAN GENOME, (SEP 1998) Vol. 9, No. 9, pp. 710-714.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.
ISSN: 0938-8990.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English

REFERENCE COUNT: 31
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Glycosylphosphatidylinositol-specific phospholipase D (GPI-PLD) is an 110-kDa monomeric **protein** found in the circulation that is capable of degrading the GPI anchor utilized by dozens of cell-surface **proteins** in the presence of detergent. This **protein** is relatively abundant (5-10 mu g/ml in **human** serum), yet its sites of synthesis, gene structure, and overall function are unclear. It is our purpose to use the mouse system to determine its putative roles in lipid transport, pathogen control, and diabetes. We have isolated murine full-length cDNA for GPI-PLD from a pancreatic alpha cell library. The deduced amino acid sequence shows 74% homology to bovine and **human** GPI-PLD. There is a single structural gene (Gpld1) mapping to mouse **Chromosome** (Chr) **13**, and among nine tissues, liver showed the greatest abundance of GPI-PLD mRNA. Genetic differences in serum GPI-PLD activity were seen among four mouse strains, and no correlation was seen between GPI-PLD activity and circulating levels of high density lipoproteins in these mice. This is the first report of map position and genetic regulation for Gpld1. This information will enable us to further study the expression and function of GPI-PLD in normal and pathological conditions.

L9 ANSWER 16 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 6

ACCESSION NUMBER: 1998285384 EMBASE
TITLE: The mouse Lect2 gene: Cloning of cDNA and genomic DNA, structural characterization and chromosomal localization.
AUTHOR: Yamagoe S.; Watanabe T.; Mizuno S.; Suzuki K.
CORPORATE SOURCE: K. Suzuki, Department of Bioactive molecules, Natl. Institute Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan. ksuzuki@nih.go.jp
SOURCE: Gene, (17 Aug 1998) 216/1 (171-178).
Refs: 14
ISSN: 0378-1119 CODEN: GENED6
PUBLISHER IDENT.: S 0378-1119(98)00294-7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We previously purified bovine leukocyte cell-derived chemotaxin 2 (LECT2) as a 16 kDa-**secreted protein** with a neutrophil chemotactic activity. LECT2 **protein** is thought to be multifunctional, since it was recently found to be identical to chondromodulin-II, a growth stimulator of chondrocyte cells. We report here the cloning and structural analysis of mouse Lect2 cDNAs and genomic DNA, and chromosomal mapping. Two types of mouse Lect2 cDNAs were cloned: one encoded the mouse counterpart of **human** and bovine LECT2 **proteins**, and the other encoded a queer type LECT2 **protein** whose amino-acid sequence in the carboxy terminus was different from that of the normal type LECT2 **protein**. The mouse Lect2 gene spanned approx. 8 kb and consisted of five exons and four introns. The

genomic organization revealed that two type transcripts arose by an alternative splicing event involving exon 4. A primer extension analysis revealed that several transcription initiation sites occurred within 60-210 nucleotides upstream from the translation initiation codon. The mouse Lect2 gene was mapped to a region adjacent to D13Mit13, D13Mit21 and Il-9 on **chromosome 13** by interspecific backcross mapping.

L9 ANSWER 17 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:464241 SCISEARCH
THE GENUINE ARTICLE: XE034
TITLE: A new family of 10 murine ovalbumin serpins includes two homologs of proteinase inhibitor 8 and two homologs of the granzyme B inhibitor (proteinase inhibitor 9)
AUTHOR: Sun J R; Ooms L; Bird C H; Sutton V R; Trapani J A; Bird P I (Reprint)
CORPORATE SOURCE: MONASH UNIV SCH MED, BOX HILL HOSP, DEPT MED, CLIVE WARD CTR, BOX HILL, VIC 3128, AUSTRALIA (Reprint); MONASH UNIV SCH MED, BOX HILL HOSP, DEPT MED, CLIVE WARD CTR, BOX HILL, VIC 3128, AUSTRALIA; AUSTIN RES INST, CELLULAR CYTOTOX LAB, HEIDELBERG, VIC 3084, AUSTRALIA
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (13 JUN 1997) Vol. 272, No. 24, pp. 15434-15441.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Serine proteinase inhibitors (serpins) are classically regulators of extracellular proteolysis, however, recent evidence suggests that some function intracellularly, Such ''ovalbumin'' serpins include the **human** proteinase inhibitors 6 (PI-6), 8 (PI-8), and 9 (PI 9), plasminogen activator inhibitor 2, and the monocyte/neutrophil elastase inhibitor, PI-9 is a potent granzyme B (graB) inhibitor that has an unusual P-1 Glu and is present primarily in lymphocytes. In a search for the murine equivalent of PI-9 we screened cDNA libraries, and performed reverse transcriptase-polymerase chain reaction on RNA isolated from leukocyte cell lines and from lymph nodes and spleens of allo-immunized mice. We identified 10 new ovalbumin serpin sequences: two resemble PI-8, two resemble PI-9, and the remaining six have no obvious **human** counterparts. Ey RNA analysis only one of the two sequences resembling PI-9 (designated SPI6) is present in mouse lymphocytes while the other (a partial clone designated mBM2A) is predominantly in testis, SPI6 comprises a 1.8-kilobase cDNA encoding a 374-amino acid **polypeptide** that is 68% identical to PI-9. mBM2A is 65% identical to PI-9 and over 80% identical to SPI6. Although the reactive loops of SPI6 and mBM2A differ from PI-9, both contain a Glu in a region likely to contain the P-1-P-1' bond. SPI6 produced in vitro using a coupled

transcription/translation system formed an SDS-stable complex with **human** graB and did not interact with trypsin, chymotrypsin, leukocyte elastase, pancreatic elastase, thrombin, or cathepsin G. Recombinant SPI6 produced in a yeast expression system was used to examine the interaction with **human**, graB in more detail. The second-order rate constant for the interaction was estimated as 8 x 10(4) M-1 s(-1), and inhibition depended on the Glu in the SPI6 reactive center, The SPI6 gene was mapped to the same region on mouse **chromosome 13** as Spi3, which encodes the murine homolog of PI-6. We conclude that even though their reactive centers are not highly conserved, SPI6 is a functional homolog of PI-9, and that the regulation of graB in the mouse may involve a second serpin encoded by mBM2A. Our identification of multiple sequence homologs of PI-S and PI-9, and six new ovalbumin serpins, is consonant with the idea that the larger set of granule and other proteinases known to exist in the mouse (compared with **human** ) is balanced by a larger array of serpins.

L9 ANSWER 18 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 7

ACCESSION NUMBER: 97289096 EMBASE
DOCUMENT NUMBER: 1997289096
TITLE: Identification and tissue expression of a splice variant for the growth arrest-specific gene gas6.
AUTHOR: Marcandalli P.; Gostissa M.; Varnum B.; Goruppi S.; Schneider C.
CORPORATE SOURCE: C. Schneider, L.N.C.I.B., AREA Science Park, Padriciano 99, 34012 Trieste, Italy. sch@icgeb.triest.it
SOURCE: FEBS Letters, (1997) 415/1 (56-58). Refs: 18 ISSN: 0014-5793 CODEN: FEBLAL
PUBLISHER IDENT.: S 0014-5793(97)01094-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The growth arrest-specific gene gas6 encodes a **secreted protein** (Gas6) which is a member of the vitamin K-dependent **protein** family and was identified as a ligand for the Axl tyrosine kinase receptor family, Gas6 shares significant similarity with **protein** S and a similar domain organisation: an extensively γ-carboxylated amino-terminal, four epidermal growth factor-like motifs and a large carboxy-terminal region, known as the D domain. Here we report on the isolation of a splice variant (gas6SV) characterised by an in-frame 129 bp insertion between the fourth EGF domain and the D domain. The gene gas6 was previously mapped on **chromosome 13**. The genomic organisation of gas6 has been investigated demonstrating the presence of alternative splicing consensus sites. Expression of gas6SV has been investigated in various **human** tissues and found to have a similar distribution pattern as gas6, with the exception of the spleen where gas6SV seems to be the predominant

form.

L9 ANSWER 19 OF 27 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 96240683 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8648639
TITLE: Tandem arrangement of the human serum albumin multigene family in the sub-centromeric region of 4q: evolution and chromosomal direction of transcription.
AUTHOR: Nishio H; Heiskanen M; Palotie A; Belanger L; Dugaiczyk A
CORPORATE SOURCE: Department of Biochemistry, University of California, Riverside 92521, USA.
SOURCE: Journal of molecular biology, (1996 May 31) 259 (1) 113-9.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U51243
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960805
Last Updated on STN: 19980206
Entered Medline: 19960725

AB The albumin gene family is comprised of four genes encoding: serum albumin (ALB), alpha-fetoprotein (AFP), alpha-albumin (ALF), and vitamin D-binding **protein** (DBP; also known as GC). The genes are regulated developmentally, expressed in the liver, and the **proteins** are **secreted** into the bloodstream. The GC gene, and the tandemly linked ALB and AFP genes, have been previously localized to **human chromosome** 4q11-**13**. Using techniques of fluorescence in situ hybridization to chromatin fibres, chromosome walking and DNA sequencing of genomic clones, we now report on the chromosomal location of the ALF gene and the organization of the entire gene family. The four genes are tandemly linked in the 4q sub-centromeric region: 5'ALB-5'AFP-5'ALF-5'GC3'-centromere, and hence are transcribed in the same, centromere-bound, direction. The linear arrangement of the four genes along the chromosome is not correlated with their temporal expression in the human ontogeny. It appears that GC is very close (and may be the gene proximal) to the centromere. The linear chromosomal arrangement of the four genes and the structural differences between them are congruent with the following evolutionary divergence of the gene family. Starting with the first duplication of an ancestral progenitor gene, a single evolutionary line led to the contemporary GC, leaving ALB/AFP/ALF on the other line of descent. The second duplication occurred in this ALB lineage, giving rise to ALB and the AFP/ALF progenitor, and the third, most recent one, gave rise to the AFP-ALF pair.

L9 ANSWER 20 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 95:459892 SCISEARCH
THE GENUINE ARTICLE: RH226
TITLE: GENE STRUCTURE, CHROMOSOMAL LOCALIZATION, AND EXPRESSION OF THE MURINE HOMOLOG OF HUMAN PROTEINASE-INHIBITOR-6 (PI-6) SUGGESTS DIVERGENCE OF

PI-6 FROM THE OVALBUMIN SERPINS

AUTHOR: SUN J R; ROSE J B; BIRD P (Reprint)
CORPORATE SOURCE: BOX HILL HOSP, CLIVE WARD CTR, MONASH MED SCH, DEPT MED, BOX HILL, VIC 3128, AUSTRALIA (Reprint); BOX HILL HOSP, CLIVE WARD CTR, MONASH MED SCH, DEPT MED, BOX HILL, VIC 3128, AUSTRALIA; UNIV MELBOURNE, DEPT ANAT & CELL BIOL, PARKVILLE, VIC 3052, AUSTRALIA
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (07 JUL 1995) Vol. 270, No. 27, pp. 16089-16096.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 27

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB **Human** proteinase inhibitor 6 (PI-6) is a recently described **protein** belonging to the serine proteinase inhibitor (serpin) superfamily. Sequence similarity suggests that PI-6 most resembles the ovalbumin (ov) serpins which include plasminogen activator inhibitor-2, the squamous cell carcinoma antigen, monocyte/neutrophil elastase inhibitor, and maspin, Although these **proteins** are associated with carcinomas and inflammation, they appear to have diverse functions and little is known of their physiological roles, In this study we have characterized cDNA and genomic clones encoding mouse PI-6 in order to analyze the localization, structure, and expression of the gene. The reactive center residues (Arg-Cys) are conserved in the mouse molecule, and recombinant mouse PI-6 was shown to bind thrombin, indicating that it has similar inhibitory properties to its **human** counterpart, Using reverse transcriptase-polymerase chain reaction assays on RNA isolated from 15-day-old embryos and adult mice, we have shown that mouse PI-6 expression is developmentally regulated, and that, unlike **human** PI-6, it is absent from the placenta, The mouse homologue of the **human** PI-6 gene has been designated Spi3 and was mapped to **chromosome 13** between the Pl1 and ctla2 alpha genes. It spans 20 kilobases, consists of 7 exons and 6 introns, and contains a TATA motif 24 nucleotides upstream of the transcriptional start site. A 680-base pair DNA fragment containing this motif and 31 nucleotides of the 5'-untranslated region of the structural gene directed transcription of a bacterial cat gene, demonstrating the presence of a functional promoter, The PI-6 gene lacks an intron present in the ovalbumin and PAI-2 genes; otherwise it is identical in terms of the numbers, position, and phasing of the intron/exon boundaries. These results suggest that PI-6 and the ov serpin genes have diverged and do not belong to the same subgroup.

L9 ANSWER 21 OF 27 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 96121306 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8557170
TITLE: Corticotropin releasing factor (CRF) binding **protein**: a novel regulator of CRF and related **peptides**.
AUTHOR: Behan D P; De Souza E B; Lowry P J; Potter E; Sawchenko P; Vale W W

CORPORATE SOURCE: Neurocrine Biosciences Inc., San Diego, California 92121, USA.
CONTRACT NUMBER: DK 07044 (NIDDK)
DK 26741 (NIDDK)
NS33426 (NINDS)
SOURCE: Frontiers in neuroendocrinology, (1995 Oct) 16 (4) 362-82. Ref: 87
Journal code: 7513292. ISSN: 0091-3022.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960312
Last Updated on STN: 19980206
Entered Medline: 19960223

AB A 37-kDa corticotropin releasing factor (CRF) binding **protein** (CRF-BP) was purified from human plasma by repeated affinity purification and subsequently sequenced and cloned. The human and rat CRF-BP cDNAs encode **proteins** of 322 amino acids with one putative signal sequence, one N-glycosylation site, and 10 conserved cysteines. Human CRF-BP binds human CRF with high affinity but has low affinity for the ovine **peptide**. In contrast, sheep CRF-BP binds human and ovine CRF with high affinity. The CRF-BP gene consists of seven exons and six introns and is located on **chromosome 13** and loci 5q of the mouse and **human** genomes, respectively. CRF-BP inhibits the adrenocorticotrophic hormone (ACTH) releasing properties of CRF in vitro. CRF-BP dimerizes after binding CRF and clears the **peptide** from blood. This clearance mechanism protects the maternal pituitary gland from elevated plasma CRF levels found during the third trimester of human pregnancy. CRF-BP is expressed in the brains of all species so far tested but is uniquely expressed in human liver and placenta. In brain, CRF-BP is membrane associated and is predominantly expressed in the cerebral cortex and subcortical limbic structures. In some brain areas CRF-BP colocalizes with CRF and CRF receptors. The **protein** is also present in pituitary corticotropes, where it is under positive glucocorticoid control, and is likely to locally modulate CRF-induced ACTH **secretion**. The ligand requirements of the CRF receptor and the CRF-BP can be distinguished in that central human CRF fragments, such as CRF (6-33) and CRF (9-33), have high affinity for CRF-BP but low affinity for the CRF receptor. The binding **protein**'s ability to inhibit CRF-induced ACTH **secretion** can be reversed by CRF (6-33) and CRF (9-33), suggesting that ligand inhibitors may have utility in elevating free CRF levels in disease states associated with decreased CRF. Thus, by controlling the amount of free CRF which activates CRF receptors, it is likely that the CRF-BP is an important modulator of CRF both in the CNS and in the periphery.

L9 ANSWER 22 OF 27 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 94296561 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8024701

TITLE: beta ig-h3: a transforming growth factor-beta-responsive gene encoding a **secreted protein** that inhibits cell attachment in vitro and suppresses the growth of CHO cells in nude mice.

AUTHOR: Skonier J; Bennett K; Rothwell V; Kosowski S; Plowman G; Wallace P; Edelhoff S; Disteche C; Neubauer M; Marquardt H; +

CORPORATE SOURCE: Bristol-Myers Squibb, Pharmaceutical Research Institute Seattle, WA 98121.

SOURCE: DNA and cell biology, (1994 Jun) 13 (6) 571-84. Journal code: 9004522. ISSN: 1044-5498.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-L19932

ENTRY MONTH: 199408

ENTRY DATE: Entered STN: 19940818
Last Updated on STN: 19970203
Entered Medline: 19940808

AB beta ig-h3 is a novel gene first discovered by differential screening of a cDNA library made from A549 human lung adenocarcinoma cells treated with transforming growth factor-beta 1 (TGF-beta 1). It encodes a 683-amino-acid **protein** containing a **secretory** signal sequence and four homologous internal domains. Here we show that treatment of several types of cells, including human melanoma cells, human mammary epithelial cells, human keratinocytes, and human fibroblasts, with TGF-beta resulted in a significant increase in beta ig-h3 RNA. A portion of the beta ig-h3 coding sequence was expressed in bacteria, and antisera against the bacterially produced **protein** was raised in rabbits. This antisera was used to demonstrate that several cell lines **secreted** a 68-kD beta IG-H3 **protein** after treatment with TGF-beta. Transfection of beta IG-H3 expression plasmids into Chinese hamster ovary (CHO) cells led to a marked decrease in the ability of these cells to form tumors in nude mice. The beta IG-H3 **protein** was purified from media conditioned by recombinant CHO cells, characterized by immunoblotting and **protein** sequencing and shown to function in an anti-adhesion assay in that it inhibited the attachment of A549, HeLa, and WI-38 cells to plastic in serum-free media. Sequencing of cDNA clones encoding murine beta ig-H3 indicated 90.6% conservation at the amino acid level between the murine and human **proteins**. Finally, the beta ig-h3 gene was localized to human chromosome 5q31, a region frequently deleted in preleukemic myelodysplasia and leukemia. The corresponding mouse beta ig-h3 gene was mapped to mouse **chromosome 13** region B to C1, which confirms a region of conservation on **human** chromosome 5 and mouse **chromosome 13**. We suggest that this **protein** be named p68 beta ig-h3.

L9 ANSWER 23 OF 27 JICST-EPlus COPYRIGHT 2004 JST on STN

ACCESSION NUMBER: 910330263 JICST-EPlus

TITLE: Isolation and characterization of new mammalian kinase genes by cross hybridization with a tyrosine

kinase probe.
AUTHOR: SHIBUYA M; MATSUSHIME H; YAMANE A; IKEDA T; TOJO A YOSHIDA M C
CORPORATE SOURCE: Univ. Tokyo, Tokyo, JPN
Hokkaido Univ., Sapporo, JPN
SOURCE: Proc Int Symp Princess Takamatsu Cancer Res Fund, (1990) vol. 20th(1989), pp. 103-110. Journal Code: X0389A (Fig. 2, Tbl. 1, Ref. 19)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
STATUS: New
AB We isolated two novel mammalian kinase genes by weak cross-hybridization with v-ros oncogene. (1) A cDNA of about 7.7kb obtained from a **human** placenta cDNA library carried a 4.2kb open reading frame, and the predicted amino acid sequence of 1338 residues contained extracellular, transmembrane and tyrosine kinase domains. The overall structure including cysteine motifs in its extracellular domain and a long **peptide** insertion in its tyrosine kinase domain indicates that this new gene is closely related to the fms family. Consequently, the gene was designated as flt(fms-like tyrosine kinase) gene. The expression of the flt gene was examined in normal and transformed cells, and it was mapped to **human chromosome** 13q12-**13**. (2) Another new gene was found to be expressed almost exclusively in testis. The cDNA sequence analysis revealed that the predicted product carried **protein** kinase consensus motifs in its amino-terminal region. Comparison of the deduced amino acid sequence of this gene in the kinase domain with those of other **protein** kinase genes will be discussed. (author abst.)

L9 ANSWER 24 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1988:70978 BIOSIS
DOCUMENT NUMBER: PREV198885037277; BA85:37277
TITLE: CHARACTERIZATION OF NORMAL AND DISEASED HUMAN COLLAGENS BY THE TECHNIQUES OF RECOMBINANT DNA.
AUTHOR(S): PIHLAJANIEMI T [Reprint author]
CORPORATE SOURCE: COLLAGEN RES UNIT, BIOCENTER OULU, DEP MED BIOCHEM, UNIV OULU, OULU, FINLAND
SOURCE: Acta Universitatis Ouluensis Series A Scientiae Rerum Naturalium, (1987) No. 189, pp. 4-58.
CODEN: AUOADB. ISSN: 0355-3191.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 27 Jan 1988
Last Updated on STN: 27 Jan 1988
AB The molecular defect in a patient with a moderately severe form of osteogenesis imperfecta was characterized. Nuclease S1 mapping revealed a homozygous mutation in the carboxyl-propeptide-coding region of the proα2(I) collagen gene in the patient. The consanguineous parents were heterozygotes for the same defect. Genomic cloning of the patient's DNA showed a four nucleotide frameshift deletion near the end of the translated region and a new termination codon four nucleotides 3' to the original one. As a

result of the deletion, the last 33 amino acids of the **protein** have an altered sequence. The abnormal primary strucutre of the carboxyl-propeptide, in turn, prevents incorporation of proα2(I) chains into a normal type I procollagen heterotrimer resulting in **secretion** of only proα (I) homotrimers. The studies directly demonstrate the critical role of carboxyl-propeptides in chain selection and assembly during the biosynthesis of procollagen. Characterization of cDNA and genomic clones coding for part of the human proα1(IV) chain provides the first complete sequence for the carboxyl-terminal globular domain of a type IV procollagen chain. A striking feature of this domain is a homology between the first and second half of the structure. The homology involved all 12 cysteine residues, the spacing between the cysteine residues, and many adjacent amino acids. This suggests that evolution of the globular domain involved duplication of an ancestral sequence coding for about 100 amino acids, six of which were cysteines. Analysis of the 3' end of the proα1(IV)gene indicates that exons coding for -Gly-X-Y-sequences vary in size between 72 bp and 134 bp, and none of them are 54 bp or multiples thereof as in the fibre forming collagen genes. Five of the six -Gly-X-Y-coding exons begin with the second base coding for glycine, and only one exon begins with a complete glycine codon as seen in the genes coding for fibre forming collagens. The introns separating the exons are large, having a total length of over 12 000 bp. The gene coding for the proα1 (IV) chain was located on **human chromosome 13**. Fibroblasts from two lethal variants of osteogenesis imperfecta were shown to synthesize increased amounts of type IV collagen. Previous studies established that one of these variants had a non-functional allele for the proα2(I) chains while the other proα2(I) allele contained a mutation leading to the synthesis of shortened proα2(I) chains. Immunofluorescent staining of the fibroblasts from the two variants indicated that a homogenous population of cells synthesized both type IV and type I procollagen. In the two variants, the relative level of mRNA for proα1(IV) was 31% and 42% of the level of mRNA for proα1(I) chains. A value of less than 2% was found for a third lethal and four non-lethal variants of osteogenesis imperfecta. The results suggest that mutations in the type I procollagen genes that result in osteogenesis imperfecta can be associated with increased expression of the genes for type IV procollagen. Four overlapping cDNA clones were characterized that code for a low molecular weight human collagen. The amino acid sequence derived from the clones resembled type IV collagen in that there were short interruptions in the repeating -Gly-X-Y-sequence. The non-collagenous, carboxyl-terminal domain was, however, much shorter and contained only 18 amino acid residues. Comparison to other collagens indicates that the collagen studied here is probably not one previously reported. Interestingly, one of the cDNA clones contained an additional 36 nucleotides not found in an overlapping clone. Nuclease S1 experiments suggested that the difference between the two cDNA clones arose from alternative splicing of RNA transcripts. Furthermore, two bacterial collagenase-sensitive **polypeptides** of Mr 67 000 and Mr 62 000 were detected in a cultured human tumour cell line, HT-1080, and in normal human skin fibroblasts with antiserum to a synthetic **peptide**

corresponding to cDNA-derived sequences.

L9 ANSWER 25 OF 27 MEDLINE on STN
ACCESSION NUMBER: 84295595 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6382024
TITLE: Localization of insulin-like growth factor genes to human chromosomes 11 and 12.
AUTHOR: Tricoli J V; Rall L B; Scott J; Bell G I; Shows T B
CONTRACT NUMBER: GM 20454 (NIGMS)
HD 05196 (NICHD)
SOURCE: Nature, (1984 Aug 30-Sep 5) 310 (5980) 784-6.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198410
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19841003

AB The insulin-like growth factors IGF-I and IGF-II are required for growth and development. Both are single-chain **proteins** (of 70 and 67 amino acids respectively) derived from precursors by proteolytic processing. IGF-I may be particularly important in promoting normal stature and IGF-II may be a fetal growth hormone. The IGF **proteins** are probably synthesized by many normal tissues and by some tumours. The **secretion** of growth factors by tumours and tumour-derived cell lines suggests that they may act as autocrine regulators of cell proliferation. Because of the possible role of these **proteins** in growth disorders and cancer, and their sequence homology with insulin, we have determined their chromosomal localization. Using somatic cell hybrids and cloned cDNA probes for these **proteins**, we have assigned the genes for IGF-I and IGF-II to human chromosomes 12 and 11, respectively. We present evidence that the IGF-II gene is located on the short arm of chromosome 11 with a ras proto-oncogene and the insulin structural gene, and also suggest the existence of a fragment length polymorphism using the IGF-I probe.

L9 ANSWER 26 OF 27 MEDLINE on STN
ACCESSION NUMBER: 84294392 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6147603
TITLE: Fetal abnormalities in cystic fibrosis suggest a deficiency in proteolysis of cholecystokinin.
AUTHOR: Gosden C M; Gosden J R
SOURCE: Lancet, (1984 Sep 8) 2 (8402) 541-6.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198410
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19950206
Entered Medline: 19841010

AB Ultrastructural and microvillous enzyme (MVE) histochemical studies

of fetuses with cystic fibrosis (CF) and trisomies 13 and 18 identified features in CF which differed from the abnormalities in trisomies 13 and 18. The principal abnormalities in CF were in the tight (occluding) junctions and intracellular organelles, particularly the golgi and mitochondria, of the epithelial cells of the pancreas, respiratory system, intestine, and gallbladder. Abnormalities of amniotic fluid MVE levels in CF and trisomy 13 occur because of disruption of the pathways by which the MVE reach the amniotic fluid. Trisomy 18 shows hypoplasia and deficiency of epithelial cell microvilli. It is postulated that the basic defect in CF is due to the deficiency of an enzyme that cleaves the Arg-Asp **peptide** bond in cholecystokinin to produce the active octapeptide CCK-8, which normally stimulates exocrine **secretion**, especially in pancreas, gallbladder, and intestine, and potentiates the action of other gastrointestinal hormones.

L9 ANSWER 27 OF 27 MEDLINE on STN
ACCESSION NUMBER: 84018018 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6604949
TITLE: Activation of human alpha 1-antitrypsin gene in rat hepatoma x human fetal liver cell hybrids depends on presence of human chromosome 14.
AUTHOR: Pearson S J; Tetri P; George D L; Francke U
CONTRACT NUMBER: CA 29617 (NCI)
GM21110 (NIGMS)
GM26105 (NIGMS)
+
SOURCE: Somatic cell genetics, (1983 Sep) 9 (5) 567-92.
Journal code: 7506054. ISSN: 0098-0366.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198311
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19831123

AB In order to study the involvement of human chromosomes in the expression of liver-specific functions, we have produced somatic cell hybrids between a rat hepatoma (7777) cell line and human diploid skin fibroblasts (series XIX) or human fetal liver cells (series XXII). Production of human serum **proteins** was detected by immunoelectrophoretic analyses of concentrated serum-free hybrid culture supernatants. Human alpha 1-antitrypsin (AAT) was **secreted** by a subset of hybrids but not by the parental cells. The activated human AAT phenotype segregated concordantly with human chromosome 14 in 18 primarily HAT-selected and five azaguanine back-selected series XXII hybrids. All other chromosomes were excluded as playing a role in AAT expression. Therefore, the AAT gene (PI) is assigned to chromosome 14. This quasi-constitutive expression of a liver-specific function was not observed for the other serum **proteins** studied, nor was it seen in the skin fibroblast-derived hybrids (series XIX) although AAT was produced by some of them.

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     FILE 'HCAPLUS' ENTERED AT 11:40:36 ON 28 APR 2004
L10             1 S ZSIG46 OR (Z SIG OR ZSIG)(W)46
L11             0 S L10 NOT L7

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 11:41:09 ON 28 APR 2004
L12             1 S L10
L13             0 S L12 NOT L8
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(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:41:33 ON 28 APR 2004)

```
L14          845 S "SHEPPARD P"?/AU
L15          437 S "GILBERTSON D"?/AU
L16           18 S L15 AND L14
L17            3 S (L14 OR L15) AND L1
L18           19 S L16 OR L17
L19           10 DUP REM L18 (9 DUPLICATES REMOVED)
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L19 ANSWER 1 OF 10 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2004-070738 [07] WPIDS

CROSS REFERENCE: 2000-687541 [67]; 2001-611088 [70]; 2002-573696 [61]; 2003-352153 [33]; 2003-874621 [81]; 2004-225671 [21]

DOC. NO. CPI: C2004-029252

TITLE: New zvegf4 polypeptides and nucleic acids, useful for diagnosing or treating cell loss or abnormal cell proliferation, e.g. cancer, treating full-thickness skin wounds or treating female reproductive tract disorders.

DERWENT CLASS: B04 D16

INVENTOR(S): GILBERT, T; **GILBERTSON, D G**; HART, C E; **SHEPPARD, P O**

PATENT ASSIGNEE(S): (GILB-I) GILBERT T; (GILB-I) GILBERTSON D G; (HART-I) HART C E; (SHEP-I) SHEPPARD P O

COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2004002140 | A1 | 20040101 | (200407)* | | 73 |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| US 2004002140 | A1 | Provisional | US 1999-132250P | 19990503 |
| | | Provisional | US 1999-164463P | 19991110 |
| | | Provisional | US 2000-180169P | 20000204 |
| | | Div ex | US 2000-564595 | 20000503 |
| | | | US 2001-876813 | 20010606 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| US 2004002140 | A1 Div ex | US 6495668 |

PRIORITY APPLN. INFO: US 2001-876813 20010606; US 1999-132250P 19990503; US 1999-164463P 19991110; US 2000-180169P 20000204; US 2000-564595 20000503

AN 2004-070738 [07] WPIDS

CR 2000-687541 [67]; 2001-611088 [70]; 2002-573696 [61]; 2003-352153 [33]; 2003-874621 [81]; 2004-225671 [21]

AB US2004002140 A UPAB: 20040418
NOVELTY - An isolated polypeptide of at least 15 amino acid residues comprises an epitope-bearing portion of a fully defined protein comprising 370 amino acids (SEQ ID NO. 2) or a sequence of amino acids having formula (I), is new.

DETAILED DESCRIPTION - An isolated polypeptide of at least 15 amino acid residues comprises an epitope-bearing portion of a fully defined protein comprising 370 amino acids (SEQ ID NO. 2) or a sequence of amino acids having formula (I), is new. The isolated polypeptide comprises a sequence of amino acids having formula (I): R1x-R2y-R3z

R1 = is a polypeptide of 100-130 residues in length, at least 70% identical to residues 52-179 of SEQ ID NO. 2, and comprises a sequence motif C(KR)Y(DNE)(WYF)X(11,15)G(KR)(WYF)C (SEQ ID NO. 4) corresponding to residues 109-131 of SEQ ID NO. 2;

R2 = is a polypeptide at least 90% identical to residues 180-257 of SEQ ID NO. 2; and

R3 = is a polypeptide at least 70% identical in amino acid sequence to residues 258-370 of SEQ ID NO. 2 and comprises a cysteine residues at positions corresponding to residues 272, 302, 306, 318, 360 or 362 of SEQ ID NO. 2, a glycine residue at a position corresponding to residue 304 of SEQ ID NO. 2 or a sequence motif CX(18,33)CXGXCX(6,33)CX(20,50)CXC (SEQ ID NO. 3) corresponding to residues 272-362 of SEQ ID NO. 2.

and each of x, y, and z is individually 0 or 1, subject to the limitations that at least one of x and z is 1 and if x and z are each 1, then y is 1.

INDEPENDENT CLAMS are also included for the following:

(1) an isolated protein comprising a first polypeptide operably linked to a second polypeptide, where the first polypeptide comprises a sequence of amino acids having formula (I), and where the protein modulates cell proliferation, apoptosis, differentiation, metabolism, or migration;

(2) an isolated polynucleotide of up to approximately 4.4 kb in length and encodes a polypeptide comprising a sequence of amino acids having formula (I);

(3) an expression vector comprising the following operably linked elements:

(a) a transcription promoter;

(b) a DNA polynucleotide; and

(c) a transcription terminator;

(4) a cultured cell into which has been introduced the expression vector and expresses the polypeptide encoded by the DNA polynucleotide;

(5) a pharmaceutical composition comprising the protein in combination with a pharmaceutical vehicle;

(6) producing the protein;

(7) an antibody that specifically binds to an epitope of the polypeptide;

(8) detecting a genetic abnormality in a patient;

(9) activating a cell-surface PDGF receptor;

(10) inhibiting a PDGF receptor mediated cellular process;

(11) stimulating the growth of bone tissue; and

(12) modulating the proliferation, differentiation, migration, or metabolism of bone cells.

ACTIVITY - Vulnerary; Gynecological; Hepatotropic;

Neuroprotective; Nootropic; Antiparkinsonian; Cytostatic. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The polypeptides, the multimeric proteins and the polynucleotides can be used in the study and regulation of cell and tissue development, as components of cell culture media and as diagnostic agents. The zvegf4 polypeptides can be used in treating of full-thickness skin wounds, including venous stasis, ulcers and other chronic, non-healing wounds, in fracture repair, skin grafting, in constructive surgery to promote neovascularization and increase skin flap survival, to establish vascular networks in transplanted cells and tissues, or in treating female reproductive tract disorders, including acute or chronic placental insufficiency and prolonged bleeding. It can also be used to promote endothelialization of vascular grafts and stents, in treating acute or chronic lesions of the gastrointestinal tract or treating or repairing liver damage. Zvegf4 can also be used for treating hepatic chronic passive congestion (CPC) and central hemorrhagic necrosis (CHN). Zvegf4 proteins, agonists and antagonists can also be used to modulate neurite growth and development and demarcate nervous system structures. It can also be used for treating peripheral neuropathies or neurodegenerative diseases including multiple sclerosis, Alzheimer's disease or Parkinson's disease. The zvegf4 polynucleotide sequence can be used to isolate polynucleotide encoding other zvegf4 proteins. They can also be used as probes or primers to clone 5' non-coding regions of a zvegf4 gene. The antibodies of the invention can be used for tagging cells that express zvegf4, for isolating zvegf4 by affinity purification, for diagnostic assays for determining circulating levels of zvegf4 polypeptides, for detecting or quantitating soluble zvegf4 as a marker of underlying pathology or disease, in analytical methods employing FACS, for screening expression libraries, for generating anti-idiotypic antibodies or as neutralizing antibodies or as agonists to block zvegf4 activity. The polypeptides, nucleic acids and antibodies can also be used to diagnose or treat disorders associated with cell loss or abnormal cell proliferation (including cancer).

Dwg.0/2

L19 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 1

ACCESSION NUMBER: 2003:163809 BIOSIS
DOCUMENT NUMBER: PREV200300163809
TITLE: Growth factor homolog zvegf3.
AUTHOR(S): Gao, Zeren [Inventor, Reprint Author]; Hart, Charles E. [Inventor]; Piddington, Christopher S. [Inventor]; **Sheppard, Paul O.** [Inventor]; Shoemaker, Kimberly E. [Inventor]; **Gilbertson, Debra G.** [Inventor]; West, James W. [Inventor]
CORPORATE SOURCE: Bellevue, WA, USA
ASSIGNEE: ZymoGenetics, Inc.
PATENT INFORMATION: US 6528050 March 04, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar 4 2003) Vol. 1268, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file.

Searcher : Shears 571-272-2528

ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Mar 2003
Last Updated on STN: 26 Mar 2003

AB Polypeptide growth factors, methods of making them, polynucleotides encoding them, antibodies to them, and methods of using them are disclosed. The polypeptides comprise an amino acid segment that is at least 90% identical to residues 46-163 of SEQ ID NO:2 or residues 235-345 of SEQ ID NO:2. Multimers of the polypeptides are also disclosed. The polypeptides, multimeric proteins, and polynucleotides can be used in the study and regulation of cell and tissue development, as components of cell culture media, and as diagnostic agents.

L19 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2
ACCESSION NUMBER: 2003:71118 BIOSIS
DOCUMENT NUMBER: PREV200300071118
TITLE: Growth factor homolog ZVEGF4.
AUTHOR(S): Gilbert, Teresa [Inventor, Reprint Author]; Hart, Charles E. [Inventor]; **Sheppard, Paul O.** [Inventor]; **Gilbertson, Debra G.** [Inventor]
CORPORATE SOURCE: Seattle, WA, USA
ASSIGNEE: ZymoGenetics, Inc.
PATENT INFORMATION: US 6495668 December 17, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec 17 2002) Vol. 1265, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB Polypeptide growth factors, methods of making them, polynucleotides encoding them, antibodies to them, and methods of using them are disclosed. Multimers of the polypeptides are also disclosed. The polypeptides, multimeric proteins, and polynucleotides can be used in the study and regulation of cell and tissue development, as components of cell culture media, and as diagnostic agents.

L19 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:832939 HCAPLUS
DOCUMENT NUMBER: 137:351520
TITLE: Novel human and mouse cytokine family proteins Zcyto20-22 and Zcyto24-25 and their class II cytokine receptor ZcytoR19, functional studies and therapeutic use thereof
INVENTOR(S): **Sheppard, Paul O.**; Fox, Brian A.; Klucher, Kevin M.; Taft, David W.; Kindsvogel, Wayne R.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002086087 | A2 | 20021031 | WO 2002-US12887 | 20020419 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002039763 | A1 | 20020404 | US 2001-895834 | 20010629 |
| US 2003104416 | A1 | 20030605 | US 2002-127816 | 20020419 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2001-285408P | P | 20010420 |
| US 2001-285424P | P | 20010420 |
| US 2001-286482P | P | 20010425 |
| US 2001-895834 | A | 20010629 |
| US 2001-341050P | P | 20011022 |
| US 2001-341105P | P | 20011022 |
| US 2000-215446P | P | 20000630 |

AB The present invention relates to polynucleotide and polypeptide mols. for Zcyto20, Zcyto21, Zcyto22, Zcyto24 and Zcyto25 proteins which are most closely related to interferon-α at the amino acid sequence level. Specifically, three human proteins Zcyto20-22 and two mouse proteins Zcyto24-25 with strong sequence homolog and their class II receptor ZcytoR19 from human are provided. The receptor for this protein family is a class II cytokine receptor, in particular protein ZcytoR19. Protein Zcyto20-22 can induce ISRE (interferon-stimulated response element) signaling, which is a signaling via interferon-response pathway interaction of type 1 interferons with their specific receptor leading to induction of a number of genes responsible for their antiviral/antiproliferative activity. The Zcyto20-22 signaling is enhanced by coexpressing ZcytoR19 and IL10Rb and is inhibited by pretreatment of recombinant cell overexpressing human ZcytoR19 with a neutralizing antibody to IL10Rb. The ability of Zcyto20, Zcyto21, Zcyto22, Zcyto24 and Zcyto25 to signal through the NF-κB signal transduction pathway was tested using a mouse monocyte/ macrophage reporter cell line. The present invention includes methods of reducing viral infections and increasing monocyte counts. The present invention also includes antibodies to the Zcyto20 polypeptides, and methods of producing the polynucleotides and polypeptides.

L19 ANSWER 5 OF 10 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-328485 [31] WPIDS
CROSS REFERENCE: 2000-423420 [36]; 2001-300278 [31]; 2002-171026 [22]; 2002-689759 [74]; 2003-370630 [35]
DOC. NO. CPI: C2003-085388
TITLE: New isolated zvegf3 polypeptide, useful for

treating cancer, Alzheimer's disease, Parkinson's disease, chronic active hepatitis, hepatic vein thrombosis, comprises growth factor domain and CUB domain.

DERWENT CLASS: B04 D16

INVENTOR(S): GAO, Z; **GILBERTSON, D G**; HART, C E; PIDDINGTON, C S; **SHEPPARD, P O**; SHOEMAKER, K E; WEST, J W

PATENT ASSIGNEE(S): (ZYMO) ZYMOGENETICS INC

COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 2002177193 | A1 | 20021128 | (200331)* | | 73 |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| US 2002177193 | A1 | Provisional | US 1998-111173P | 19981207 |
| | | Provisional | US 1999-142576P | 19990706 |
| | | Provisional | US 1999-161653P | 19991021 |
| | | Provisional | US 1999-165255P | 19991112 |
| | | Div ex | US 1999-457066 | 19991207 |
| | | | US 2002-139583 | 20020502 |

PRIORITY APPLN. INFO: US 2002-139583 20020502; US 1998-111173P 19981207; US 1999-142576P 19990706; US 1999-161653P 19991021; US 1999-165255P 19991112; US 1999-457066 19991207

AN 2003-328485 [31] WPIDS

CR 2000-423420 [36]; 2001-300278 [31]; 2002-171026 [22]; 2002-689759 [74]; 2003-370630 [35]

AB US2002177193 A UPAB: 20030603

NOVELTY - An isolated mouse or human polypeptide comprising:

(a) polypeptide segment 100-120 amino acids long that is 90% identical to amino acid residues 46-163 (CUB domain) of fully defined zvegf3 polypeptide sequence of 345 amino acids (S1) as given in specification;

(b) polypeptide segment that is 90% identical to residues 164-234 of S1; and

(c) polypeptide segment that is 90% identical to residues 235-245 (growth factor domain) of S1, is new.

DETAILED DESCRIPTION - An isolated mouse or human polypeptide (I) comprising a sequence of amino acids of the formula R1x-R2y-R3, where:

R1 = a polypeptide of 100-120 residues in length that is at least 90% identical to residues 46-163 of S1, and comprises a sequence motif C(KR)Y(DNE)(WYF)X(11,15)G(KR)(WYF)C corresponding to residues 104-124 of S1;

R2 = a polypeptide at least 90% identical to residues 164-234 of S1;

R3 = a polypeptide at least 90% identical in amino acid sequence to residues 235-345 of S1 and comprises cysteine residues at positions corresponding to residues 250, 280, 284, 296, 335 and 337 of S1, a glycine residue at a position corresponding to residue 282 of S1, and a sequence motif CX(18,33)CXGXCX(6,33)CX(20,40)CXC corresponding to residues 250-337 of S1;

x, y and z = individually 0 or 1, subject to the limitations that: at least one of x and z is 1, and if x and z are each 1, then y is 1.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (II) of at least 15 amino acid residues comprising an epitope-bearing portion of (S1) or of a fully defined sequence of 345 amino acid residues as given in the specification;

(2) an isolated protein (III) comprising, a first polypeptide operably linked to a second polypeptide;

(3) producing (I);

(4) an isolated polynucleotide (IV) of up to approximately 4 kb in length, where the polynucleotide encodes (I);

(5) an expression vector (V) comprising the following operably linked elements: a transcription promoter, (IV) and a transcription terminator;

(6) a cultured cell (VI) which has been introduced (V), where the cell expresses the polypeptide encoded by the DNA segment;

(7) an antibody (VIII) that specifically binds to an epitope of (I);

(8) detecting (M1) a genetic abnormality in a patient;

(9) inhibiting (M2) a platelet-derived growth factor (PDGF) alpha receptor mediated cellular process;

(10) inhibiting zvegf3 activity in a mammal involves administering to the mammal an effective amount of zvegf3 antagonist;

(11) an isolated, antisense polynucleotide (IX) that is the complement of (IV);

(12) decreasing zvegf2 activity in a mammal, by administering to the mammal an effective amount of an antibody (X) that specifically binds to an epitope of a polypeptide consisting of a sequence of amino acid residues 230-345, 231-345, 232-345, 233-345, 234-345, 235-345, 236-345, 237-345, 238-345, 239-345 or 240-345 of (S1); and

(13) decreasing zvegf3 activity in a mammal by administering to a mammal, an antibody (XI) that specifically binds to a dimeric protein having two polypeptide chains where each polypeptide chain consists of residues 230-345, 231-345, 232-345, 233-345, 234-345, 235-345, 236-345, 237-345, 238-345, 239-345 or 240-345 of (S1).

ACTIVITY - Cytostatic; Hepatotropic; Antiinflammatory; Thrombolytic; Vulnerary; Tranquilizer; Cerebroprotective; Neuroprotective; Nootropic; Antiparkinsonian; Antidiabetic; Ophthalmological; Antipsoriatic; Antiarthritic; Dermatological; Antirheumatic; Coagulant; Antiulcer; Cardiant. Thirty mice (male, c57BL6) were each injected subcutaneously with 2.5 multiply 10 to the power of 5 Lewis lung carcinoma cells. Three days after implantation of cells, the mice were split into three groups of ten and were injected with either saline, zvegf3 adenovirus (1 multiply 10 to the power of 11 particles), or control adenovirus (1 multiply 10 to the power of 11 particles). Growth of tumors was monitored by

dimensional measurement on day 14 and by gross tumor weight at the time of sacrifice (day 21). Lungs, liver and tumor were examined by histological methods. Tumor size was significantly lower in the zvegf3-treated group compared to the control adenovirus group. The incidence of metastasis was low and did not differ among the groups.

MECHANISM OF ACTION - Cell proliferation, migration, differentiation or metabolism, modulator; organ development and regeneration regulator; PDGF alpha receptor agonist; Modulator of neurite growth and development; Gene therapy.

USE - (III) is useful for stimulating the growth of fibroblasts or smooth muscle cells, or for activating a cell-surface PDGF alpha receptor which involves exposing a cell comprising a cell-surface PDGF alpha receptor to (III). (IX) is useful for inhibiting zvegf3 production in a cell (claimed). The protein is useful as a PDGF alpha receptor agonist and thus is useful for treating full-thickness skin wounds, female reproductive tract and prolonged bleeding, periodontal disease, damaged liver tissue, and duodenal ulcers. The polypeptides are also useful additives in tissue adhesives for promoting revascularizing of the healing tissue. (I) is also useful for treating liver damage including damage due to liver disease, chronic active hepatitis and many types of cirrhosis. zvegf3 may also be useful for the treatment of hepatic chronic passive congestion (CPC) and central hemorrhagic necrosis (CHN). (I) is also useful for treating hepatic vein thrombosis, portal vein thrombosis, and cardiac sclerosis. (I) is useful for enhancing expansion and mobilization of endothelial precursor stem cells, creating and stabilizing new vessel formation in areas requiring neovascularization, including areas of ischemia, organ transplants, wound healing, and tissue grafting. (I) is useful for treating peripheral neuropathies by increasing spinal cord and sensory neurite outgrowth, and as part of therapeutic treatment for the regeneration of neurite outgrowths following strokes, brain damage caused by head injuries, and paralysis caused by spinal injuries. Application may also be made in treating neurodegenerative diseases such as multiple sclerosis, Alzheimer's disease and Parkinson's disease. (VIII) (zvegf3 antagonist) is useful for treating diabetic retinopathy, psoriasis, arthritis, and scleroderma, and reducing fibrosis, keloids, liver fibrosis, lung fibrosis, kidney fibrosis, and glomerulosclerosis. (VIII) is useful for blocking the mitogenic, chemotactic, or angiogenic effects of zvegf3, and for treating proliferative vascular disorders. (VIII) is useful for treating ocular neovascularization, inflammatory disorders, rheumatoid arthritis and psoriasis. (I), (IV) and (VIII) are useful for diagnosis and treatment of cancer, impaired or excessive vasculogenesis or angiogenesis and diseases of the nervous system. Dwg.0/6

L19 ANSWER 6 OF 10 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-689759 [74] WPIDS
CROSS REFERENCE: 2000-423420 [36]; 2001-300278 [31]; 2002-171026 [22]; 2003-328485 [31]; 2003-370630 [35]
DOC. NO. CPI: C2002-194896
TITLE: Novel polypeptide, designated zvegf3 useful for treating skin wounds, ulcers, burns, skin grafting, female reproductive tract disorders, Parkinson's disease, and Alzheimer's disease.

DERWENT CLASS: B04 D16
INVENTOR(S): GAO, Z; **GILBERTSON, D G**; HART, C E; PIDDINGTON, C S; **SHEPPARD, P O**; SHOEMAKER, K E; WEST, J W
PATENT ASSIGNEE(S): (ZYMO) ZYMOGENETICS INC
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| US 6432673 | B1 | 20020813 | (200274)* | | 68 |

APPLICATION DETAILS:

| PATENT NO | KIND | | APPLICATION | DATE |
|---|---|---|---|---|
| US 6432673 | B1 | Provisional | US 1998-111173P | 19981207 |
| | | Provisional | US 1999-142576P | 19990706 |
| | | Provisional | US 1999-161653P | 19991021 |
| | | Provisional | US 1999-165255P | 19991112 |
| | | | US 1999-457066 | 19991207 |

PRIORITY APPLN. INFO: US 1999-457066 19991207; US 1998-111173P 19981207; US 1999-142576P 19990706; US 1999-161653P 19991021; US 1999-165255P 19991112

AN 2002-689759 [74] WPIDS
CR 2000-423420 [36]; 2001-300278 [31]; 2002-171026 [22]; 2003-328485 [31]; 2003-370630 [35]
AB US 6432673 B UPAB: 20030603
NOVELTY - An isolated polypeptide (I), designated zvegf3 which is 111-136 amino acid residues in length and comprises a sequence (S1) of 345 amino acids fully defined in the specification, from amino acid residues 235-345, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an isolated protein (II) comprising a first polypeptide disulfide bonded to a second polypeptide, where each of the first and second polypeptides is (I), and where the protein modulates cell proliferation, differentiation, metabolism or migration;

(2) a composition (III) comprising (II);

(3) an isolated polynucleotide (IV) encoding (I);

(4) an expression vector (V) comprising (IV), a transcription promoter and a transcription terminator, which are operably linked to each other;

(5) a cultured cell (VI) into which (V) has been introduced, expresses the polypeptide encoded by the DNA segment; and

(6) producing (II).

ACTIVITY - Antidiabetic; Ophthalmological; Antipsoriatic; Antirheumatic; Antiarthritic; Cytostatic; Antiatherosclerotic; Immunosuppressive; Antiinflammatory; Dermatological; Vulnerary; Nephrotropic; Hepatotrophic; Cardiant; Neuroprotective; Antiparkinsonian; Nootropic; Cerebroprotective; Vasotropic.

The anti-tumor effect of zvegf3 adenovirus on c57BL6 male mice

was evaluated. Thirty mice were each injected subcutaneously with 2.5 multiply 105 Lewis lung carcinoma cells. Three days after implantation of cells, the mice were split into three groups of ten and were injected with either saline, zvegf3 adenovirus (1 multiply 1011 particles), or control adenovirus (1 multiply 1011 particles). Growth of tumors was monitored by dimensional measurement on day 14 and by gross tumor weight at the time of sacrifice (day 21). Lungs, liver and tumor were examined by histological methods. Tumor size was significantly lower in the zvegf3-treated group compared to the control adenovirus group.

MECHANISM OF ACTION - Modulator of cell proliferation, differentiation, metabolism or migration (claimed); Gene therapy.

USE - (I) Is useful as additives in tissue adhesives for promoting revascularization of the healing tissue, for designing molecules that antagonize semaphorin-stimulated activities, including neurite growth, cardiovascular development, cartilage and limb development, and T and B-cell function, and for imaging tumors or other sites of abnormal cell proliferation and in gene therapy applications.

(II) Is useful therapeutically to stimulate tissue development or repair, or cellular differentiation or proliferation, and for stimulating the growth of fibroblast or smooth muscle cells. (II) is also useful as molecular weight standards, as reagents in assays for determining circulatory level of the protein or as standards in the analysis of cell phenotype; for identifying inhibitors of their activity which are useful for reducing the growth of solid tumors, for treating diabetic retinopathy, psoriasis, rheumatoid arthritis, various forms of cancers, autoimmune disease, inflammation, myocardial ischemia, scleroderma, and reducing fibrosis, including scar formation, keloids, liver fibrosis, lung fibrosis (e.g. silicosis, abestosis), kidney fibrosis (including diabetic nephropathy), glomerulosclerosis and atherosclerosis; and for identifying cells, tissues or cell lines that respond to a zvegf3-stimulated pathway.

(I) And (II) are useful for activating a cell surface platelet-derived growth factor alpha (PDGF alpha ) receptor which is useful for treating skin wounds, ulcers, burns, skin grafting, and female reproductive tract disorders; for raising antibodies which are useful for monitoring protein expression and isolation, and in detecting zvegf3 proteins or in immunoprecipitation studies; and for treating or repairing tissue damage due to chronic liver disease (hepatitis), cirrhosis, Reye's syndrome, Wilson's disease, circulatory disorders e.g. heart failure, hepatic or portal vein thrombosis, and cardiac sclerosis, neurodegenerative diseases such as multiple sclerosis, Parkinson's disease, Alzheimer's disease, and for regenerating neurite outgrowths following strokes.

(I) And (IV) are useful for studying and regulating cell and tissue development, as components of cell culture medium, and as diagnostic agents. (IV) is useful for isolating polynucleotides encoding other zvegf3 proteins, as probes or primers to clone 5' non-coding regions of zvegf3 gene, and for detecting genetic abnormality in a patient.

Dwg.0/6

L19 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2001:549111 HCAPLUS

DOCUMENT NUMBER: 135:237032
TITLE: Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF α and β receptor
AUTHOR(S): **Gilbertson, Debra G.**; Duff, Meghan E.; West, James W.; Kelly, James D.; **Sheppard, Paul O.**; Hofstrand, Philip D.; Gao, Zeren; Shoemaker, Kimberly; Bukowski, Thomas R.; Moore, Margaret; Feldhaus, Andrew L.; Humes, Jacqueline M.; Palmer, Thomas E.; Hart, Charles E.
CORPORATE SOURCE: ZymoGenetics Inc., Seattle, WA, 98102, USA
SOURCE: Journal of Biological Chemistry (2001), 276(29), 27406-27414
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have characterized platelet-derived growth factor (PDGF) C, a novel growth factor belonging to the PDGF family. PDGF-C is a multidomain protein with the N-terminal region homologous to the extracellular CUB domain of neuropilin-1, and the C-terminal region consists of a growth factor domain (GFD) with homol. to vascular endothelial growth factor (25%) and PDGF A-chain (23%). A serum-sensitive cleavage site between the two domains allows release of the GFD from the CUB domain. Competition binding and immunopptn. studies on cells bearing both PDGF α and β receptors reveal a high affinity binding of recombinant GFD (PDGF-CC) to PDGF receptor-α homodimers and PDGF receptor-α/β heterodimers. PDGF-CC exhibits greater mitogenic potency than PDGF-AA and comparable or greater mitogenic activity than PDGF-AB and PDGF-BB on several mesenchymal cell types. Anal. of PDGF-CC in vivo in a diabetic mouse model of delayed wound healing showed that PDGF-CC significantly enhanced repair of a full-thickness skin excision. Together, these studies describe a third member of the PDGF family (PDGF-C) as a potent mitogen for cells of mesenchymal origin in in vitro and in vivo systems with a binding pattern similar to PDGF-AB.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2000:790635 HCAPLUS
DOCUMENT NUMBER: 133:345605
TITLE: Protein and cDNA sequences of novel human and mouse vascular endothelial growth factor zvegf-4 and diagonistic and therapeutic uses thereof
INVENTOR(S): Gilbert, Teresa; Hart, Charles E.; **Sheppard, Paul O.**; **Gilbertson, Debra G.**
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000066736 | A1 | 20001109 | WO 2000-US40047 | 20000503 |
| WO 2000066736 | B1 | 20001221 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1177293 | A1 | 20020206 | EP 2000-928993 | 20000503 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002542825 | T2 | 20021217 | JP 2000-615760 | 20000503 |
| US 2003105015 | A1 | 20030605 | US 2002-226559 | 20020823 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1999-304216 | A | 19990503 |
| US 1999-164463P | P | 19991110 |
| US 2000-180169P | P | 20000204 |
| US 1999-132250P | P | 19990503 |
| US 2000-540224 | A3 | 20000331 |
| WO 2000-US40047 | W | 20000503 |

AB The present invention provides protein and cDNA sequences for a newly identified human and mouse vascular endothelial growth factor, designated zvegf-4, which is cloned from a human chronic myelogenous leukemia cell and mouse genomic library by its homol. to the VEGF family. The vascular endothelial growth factor zvegf-4 resides on human chromosome 11 at 11q22.3-q23.1. The invention also relates to the tissue distribution of zvegf-4 mRNA. The present invention also includes antibodies to zvegf-4. The sequences of zvegf-4, may be used for detecting human disease associated with zvegf-4 activities, and as a therapeutic.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:401998 HCAPLUS
DOCUMENT NUMBER: 133:38714
TITLE: ZVEGF3: a homolog of vascular endothelial growth factor and its use
INVENTOR(S): Gao, Zeren; Hart, Charles E.; Piddington, Christopher S.; **Sheppard, Paul O.**; Shoemaker, Kimberly E.; **Gilbertson, Debra G.**; West, James W.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000034474 | A2 | 20000615 | WO 1999-US28968 | 19991207 |
| WO 2000034474 | A3 | 20001228 | | |
| WO 2000034474 | C2 | 20020829 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1137773 | A2 | 20011004 | EP 1999-966032 | 19991207 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002531127 | T2 | 20020924 | JP 2000-586908 | 19991207 |
| AU 764039 | B2 | 20030807 | AU 2000-21679 | 19991207 |
| US 6528050 | B1 | 20030304 | US 2000-706968 | 20001106 |
| US 2003087870 | A1 | 20030508 | US 2002-264361 | 20021003 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1998-207120 | A | 19981207 |
| US 1999-142576P | P | 19990706 |
| US 1999-161653P | P | 19991021 |
| US 1999-165255P | P | 19991112 |
| US 1998-111173P | P | 19981207 |
| US 1999-457066 | A2 | 19991207 |
| WO 1999-US28968 | W | 19991207 |
| US 2000-541752 | A1 | 20000331 |
| US 2000-222223P | P | 20000801 |
| US 2000-695121 | A1 | 20001023 |

AB A protein that shows sequence similarities to the vascular endothelial growth factors and that may be of therapeutic use is identified and characterized using them are disclosed. The polypeptides comprises an amino acid segment that is at least 90% identical to residues 46-163 of SEQ ID NO:2 or residues 235-345 of SEQ ID NO:2. Multimers of the polypeptides are also disclosed. The polypeptides, multimeric proteins, and polynucleotides can be used in the study and regulation of cell and tissue development, as components of cell culture media, and as diagnostic agents. The gene was identified in public EST databases and a cDNA cloned by PCR from a human salivary gland cDNA library. Ectopic expression of the gene in transgenic mice using inducible promoters resulted in abnormalities of the liver, spleen and hematopoiesis. Similarly, mice infected with an adenovirus carrying the gene had enlarged livers with sinusoidal cell proliferation. The spleen was similarly affected and the mice showed abnormalities in platelet counts. The protein stimulated aortal outgrowth in vitro about as effectively as other growth factors tested with fibroblasts and smooth muscle cells being the most affected. The protein stimulated intracellular calcium release in these cells.

L19 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1999:96357 HCAPLUS

DOCUMENT NUMBER: 130:164008
TITLE: Cloning and cDNA sequence of secreted protein zsig46 encoded by **human chromosome 13**
INVENTOR(S): **Sheppard, Paul O.; Gilbertson, Debra G.**
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9905275 | A1 | 19990204 | WO 1998-US15431 | 19980724 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9885898 | A1 | 19990216 | AU 1998-85898 | 19980724 |
| EP 1002077 | A1 | 20000524 | EP 1998-937110 | 19980724 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001511345 | T2 | 20010814 | JP 2000-504249 | 19980724 |
| US 2002042093 | A1 | 20020411 | US 1998-122383 | 19980724 |
| US 2002173624 | A1 | 20021121 | US 2001-10050 | 20011109 |

PRIORITY APPLN. INFO.: US 1997-53613P P 19970724
US 1998-122383 A1 19980724
WO 1998-US15431 W 19980724

AB The present invention relates to polynucleotide and polypeptide mols. a for zsig46 polypeptide, a novel secreted protein located on **human chromosome 13**. The zsig46 polypeptides were initially identified by querying an EST database for secretory signal sequences, characterized by an upstream methionine start site, a hydrophobic region of .apprx.13 amino acids and a cleavage site, in an effort to select for secreted proteins. Eight potential N-glycosylation sites and are located on zsig46, and potential post-translational processing sites are the dibasic sites at amino acids 38-39, 46-47, and 277-278. The mRNA corresponding to zsig46 is expressed predominantly in thyroid. The zsig46 polypeptides, and polynucleotides encoding them, are secreted proteins and may be used in the study of receptors for which a ligand has not yet been identified, of secretory pathways and the like. The present invention also includes antibodies to the zsig46 polypeptides.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE' ENTERED AT 11:45:54 ON 28 APR 2004)

| | | | | | |
|---|---|---|---|---|---|
| L20 | 2334 | SEA FILE=MEDLINE | ABB=ON | PLU=ON | "CHROMOSOMES, HUMAN, PAIR 13"/CT |
| L21 | 124239 | SEA FILE=MEDLINE | ABB=ON | PLU=ON | PROTEINS/CT |
| L22 | 104 | SEA FILE=MEDLINE | ABB=ON | PLU=ON | POLYPROTEINS/CT |
| L23 | 32 | SEA FILE=MEDLINE | ABB=ON | PLU=ON | L20 AND (L21 OR L22) |
| L24 | 4634 | SEA FILE=MEDLINE | ABB=ON | PLU=ON | POLYNUCLEOTIDES/CT |
| L25 | 0 | SEA FILE=MEDLINE | ABB=ON | PLU=ON | L23 AND L24 |

FILE 'HOME' ENTERED AT 11:48:58 ON 28 APR 2004